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# THE LERICHE SYNDROME (THROMBOTIC OBLITERATION OF THE AORTIC BIFURCATION)*

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THROMBOTIC obliteration of the aortic bifurcation, which is insidious in onset and gives rise to a complete and chronic occlusion, is very rarely reported. However, that it is not an exceedingly rare lesion is shown by its incidence of approximately 1 in 1,000 cases in a study of 5,350 autopsies[2] and in another series of 6,547 autopsies it was found 11 times.[9]

Chronic thrombotic obliteration should be distinguished from acute embolic occlusion of the aortic bifurcation. These latter may originate from the left side of the heart (intracardiac thrombi, mural thrombi or valvular vegetations), from thrombi in the pulmonary veins, or from a thrombus higher in the aorta, *i.e.*, in an aortic aneurysm. The usual clinical picture of occlusion at the aortic bifurcation, due to an embolus, giving rise to the so-called saddle embolus, is that of a sudden onset with acute severe symptoms and violent pain. Because of the lack of time for an adequate collateral circulation to develop, paraplegia, shock, and ascending gangrene rapidly lead to death unless the clot is removed by surgical intervention. Embolic occlusion of the terminal aorta gives a symptom complex which is measured by hours and days; thrombotic occlusion extends over a period of years. The differential is adequate time to develop efficient collateral channels.

Thrombotic obliteration of the aortic bifurcation has long been recognized as a distinct pathologic entity. Welch,[11] in his classic study of thrombosis and embolism of the abdominal aorta in 1899, cites case reports by Graham in 1814, and by Barth in 1848. Welch himself reviewed 59 reported cases, but only 7 were primarily thrombotic. In 1923 Leriche[3] reported on this lesion, and again in 1940 he[4] described the symptom complex and diagnostic criteria, with details of 5 cases in which the diagnosis was proved at operation.

Because of the many significant experimental and clinical contributions to the

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study of arterial diseases by the distinguished French surgeon, Leriche, the syndrome of thrombotic obliteration of the aortic bifurcation has been named in his honor. Among the most informative recent descriptions of this syndrome are those by Leriche and Morel[5] in 1948, and in 1949 by Elkin and Cooper.[1]

As clinicians become more aware of this insidious syndrome, radiologists will be called upon with increasing frequency to help in establishing a diagnosis. By means of abdominal aortography the radiologist can be prepared to offer information as to:

1. The site of the lesion. One of the recommended procedures in the treatment of this disease is surgical removal of the thrombosed areas, wherever practicable, as this may prevent the continued formation of clots. Hence, in the planning of precise surgery, it is of obvious importance to outline the site of thrombosed vessels, which can only be done by abdominal aortography.

2. The extent of the lesion. Visualization of the extent of the lesion gives information as to the feasibility of surgical intervention. Thus, if aortograms show the thrombosis to involve the renal arteries, resection is contraindicated due to the present lack of surgical techniques for maintaining an adequate blood supply to the kidneys.

3. The state of collateral circulation present. This information is of prognostic significance, and might possibly also be a visual aid in estimating the results of a lumbar sympathectomy. It should be realized, however, that visualization of the collateral circulation does not offer as much information as the exercise or walking tolerance of a lower extremity in estimating the efficacy of collateral circulation present.

## ETIOLOGY AND PATHOLOGY

Complete occlusion of the terminal abdominal aorta may occur by thrombosis in sites associated with (1) ulcerated atherosclerotic plaque, (2) arteritis of the abdominal aorta, (3) dissecting aneurysm of the aorta, and (4) congenital narrowing or extrinsic pressure, with narrowing of the aorta. The latter two etiologic factors may lead to secondary thrombotic involvement, but the Leriche syndrome is concerned with primary thrombotic involvement of the terminal aortic region.

Two views are currently being proposed: that favored by Leriche holds that it is an inflammatory lesion—a true arteritis; the other view maintains that the condition arises principally on the basis of an atherosclerosis.

In favor of an arteritis are the following considerations:

1. The fact that the thrombotic obliteration is relatively rare, and advanced atheromatous changes, particularly at the terminal abdominal aorta, are very common.

2. Thrombotic obliteration often begins in one of the common iliac arteries, whereas atherosclerosis is usually most marked at the terminal aorta.

3. The occasional occurrence of the lesion in relatively young people (Leriche reported a twenty-nine year old patient), without evidence of other atheromatous arterial disease.

4. The report of cases with diffuse vascular disease, the aortic thrombosis appearing to be a mere incident in the course of a progressive disease, involving the entire arterial tree with an arteritis (Case VI in a thirty-eight year old male, reported by Gross and Philips[2]).

5. Leriche has reported, and we have also found in 3 of our 6 cases, that often, around the affected vessels, there is an intensive periarteritis, which attaches the vessel to surrounding structures, sometimes involving the neighboring veins and lymphatics.

In favor of an atherosclerotic etiology, which suggests that the thrombus forms on an ulcerated intima associated with an atheromatous plaque, there are the following factors:

1. The very high incidence of atheromatous changes at the aortic bifurcation.

This consideration is only valid for those cases in which the lesion starts at the terminal aorta.

2. In about a third of the cases reported there was an antecedent history of coronary disease on an arteriosclerotic basis (3 out of 6 cases reported in this series had coronary artery disease).

3. The Leriche syndrome is insidious in onset and slowly progresssive, in contrast to an arteritis, which usually is more abrupt in onset and rapid in its course.

4. Fever and leukocytosis have not been reported in cases of the Leriche syndrome, which might be expected in an arteritis.

5. If the etiology were inflammatory, some of these cases should be accompanied by evidence of vessel necrosis, which does not occur.

The microscopic findings do not have the features of a specific histopathology—"pas de signature histologique specifique" (Martin). They may represent an inflammatory response to the formation of a thrombus on an ulcerated atheromatous plaque, or they may be indicative of an arteritis.

The final decision as to the etiology should be left open, pending the collection of additional evidence.

The thrombus often begins in one of the common iliac arteries (as demonstrated in Fig. 4, Case I, and Fig. 11, Case VI). The lesion then extends upward, reaching the terminal aorta, and then the opposite common iliac artery becomes involved. Whatever the mode of origin, the thrombosis finally obliterates the terminal aorta, and both common iliac arteries and their branches, which become hard and cord-like. The thrombosis continues to extend both upward and downward. The inferior mesenteric artery is not uncommonly involved (Fig. 6, Case III), and sometimes the terminal picture is due to involvement of the renal artery orifices.

### CLINICAL FINDINGS AND DIAGNOSIS

This disease shows a great preponderance in males. In a review of 47 cases reported since 1940, 43 were males, and the majority occurred in patients forty-five to sixty-five years old. However, Leriche reported a case in a twenty-nine year old male. Our cases have an average age of fifty-six years, the youngest being forty-seven.

Three of our 6 patients had hypertension. However, in 2 of these cases (Fig. 4, Case I, and Fig. 11, Case VI) the abdominal aortograms showed only early involvement of the common iliacs, and it appears unlikely that the disease process is an etiological factor of the hypertension. When the thrombus involves the renal artery orifices a resultant hypertension may be anticipated.

It is important to point out that this syndrome has an insidious onset. Many clinicians are unaware that thrombosis, with chronic occlusion of the aortic bifurcation and common iliac arteries, may occur without rapid gangrene of the lower extremities, because of compensatory collateral circulation. The symptoms may increase slowly over a period of years. Since this syndrome has a fairly typical chain of signs and symptoms, a high index of suspicion should make the diagnosis fairly easy. The symptoms are:

1. Easy fatigability of the lower extremities; a sense of weakness or extreme weariness appears after walking.

2. Pain in the hips, thighs and calves on exertion.

3. In the male, inability to maintain a stable erection; this occurs in about one-third of the cases, and is said to be caused by vasospasm of the major pelvic arteries, resulting in relative ischemia of the corpora cavernosa.

4. A sensation of coldness in the lower extremities. Findings on physical examination are:

1. Absence of peripheral arterial pulsations, including the femoral; there may also be absence of abdominal aortic pulsations below the umbilicus.

2. Systolic murmurs over the aortic bifurcation, as well as over the external iliac arteries. These murmurs are probably due to segmental narrowing of the aorta and

iliacs by atherosclerotic plaques with superimposed thrombi, or by an area of arteritis with thrombus formation.

3. Pallor of the skin of the legs and feet, even when standing; when the legs are raised to the vertical the pallor becomes ivory-like.

4. Symmetrical atrophy of the musculature of both lower extremities, which Leriche calls a global atrophy. This is a symmetrical process, and may be easily overlooked, as there is no normal limb as a basis for comparison.

5. Trophic changes of the skin and toenails, and gangrene, usually appear in the terminal stages of the disease.

Some other clinical data on the patients observed are presented in Table 1.

TABLE I

CLINICAL DATA IN SIX PATIENTS WITH THE LERICHE SYNDROME

| Case | Age | Sex | Duration of Symptoms in Years | Loss of Stable Erection | History of Coronary Disease | Blood Pressure | Periarterial Adhesions Found at Operation |
|---|---|---|---|---|---|---|---|
| I | 57 | M | ½ | + | NP | 160/92 | NP |
| II | 62 | M | 2 | NP | + | 160/76 | NP |
| III | 50 | M | 3 | NP | + | 120/65 | + |
| IV | 58 | M | 6 | NP | NP | 160/100 | NP |
| V | 47 | M | 5 | + | + | 142/80 | + |
| VI | 63 | M | 2½ | + | NP | 180/102 | + |

+ =Symptom or finding present.
NP =Symptom or finding not present.

Instrumental observations, such as skin temperatures and oscillometry, may be used to confirm the physical findings. Ballistocardiography has also been used as a diagnostic procedure;[1] however, since it merely records waves which may be aberrated by any obstructive lesion anywhere in the descending thoracic aorta and below, it does not furnish information as to the site and extent of a thrombotic lesion.

Abdominal aortography should be performed to confirm the diagnosis, fix the site, and outline the extent of the thrombosis.

## ABDOMINAL AORTOGRAPHY

The technique of the procedure of abdominal aortography may be briefly outlined as follows:

The patient is placed in the prone position on the roentgenographic table. A 14 by 17 inch preliminary film is made to check on the positioning and roentgen technique (Fig. 1). The patient is anesthetized with sodium pentothal. An 18 gauge, 6 inch, needle is inserted at the lower edge of the twelfth rib, about 8 cm. to the left of the midline (Fig. 1). The contrast medium may be 80 per cent sodium iodide or 70 per cent diodrast. With either contrast medium, 10 to 12 cc. is injected in about three seconds, and the film is exposed as the last centimeter is injected. The length of exposure should be the shortest possible within the capacity of the machine. Films of good quality can be obtained in the average patient with a 200 ma. machine, using 80 to 90 kv., 200 ma., and 1/10 to 3/20 second exposure time, with a target-film distance of 36 inches, using a high speed Potter-Bucky diaphragm, par-speed screens, and fast film.

Further details as to the equipment needed, technique of inserting the needle, possible complications, and after-care, may be obtained elsewhere.[7,8,10]

A normal abdominal aortogram is shown in Figure 2, and a composite drawing of the usual relationship of vessels, which may be visualized by this procedure in normal subjects, is shown in Figure 3.

That abdominal aortography is not a significantly dangerous procedure is evidenced by the report of Melick and Vitt,[6] who, in a review of the literature up to 1948, could not find a single fatality in the 3,000 cases reported. To date, we have not

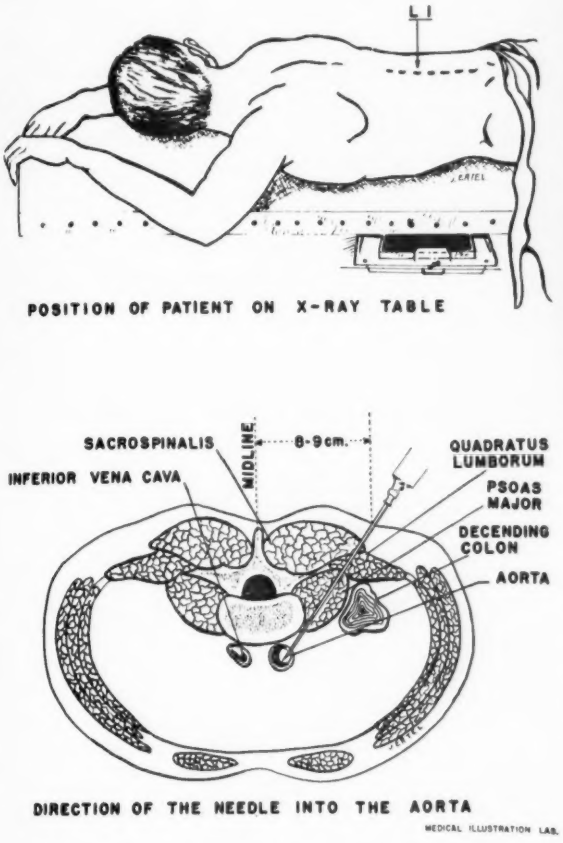


Fig. 1. Technique of abdominal aortography. A 14 by 17 inch film lengthwise is used.

been able to find any fatalities reported. However, we have had several serious accidents; in one case the splenic artery was directly injected, with a resulting symptom complex of a splenectomy; in another case, the superior mesenteric artery was directly injected. Even though it may be anticipated that abdominal aortography will be employed with increasing frequency, and some fatalities may occur, it will probably remain less dangerous than cardiac or cerebral angiography.

Leriche[5] advises that patients who show (a) marked overweight, (b) signs of cardiac failure, and (c) cyanosis of the feet and legs, with violaceous blurs, even though the diagnosis of thrombosis is suspected, should not undergo abdominal aortography. In such instances, the procedure may lead to fatal extension of the arterial thrombosis.

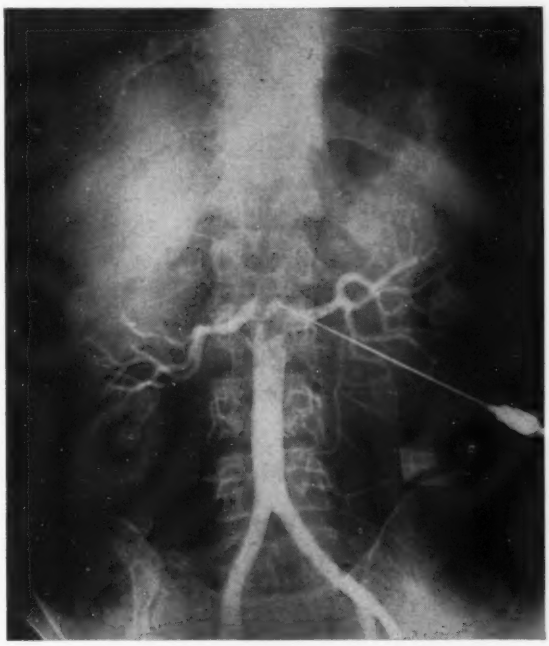

Fig. 2. Normal abdominal aortogram. There is good visualization of the lower lumbar arteries and the right inferior phrenic artery.

## PROGNOSIS AND TREATMENT

The duration of symptoms in our 6 cases varied from six months to six years. The insidious chronic occlusion may be well borne for a number of years, depending on the efficacy of the collateral circulation established. However, the underlying nature of the disease makes the prognosis grave, whatever the method of treatment. Death usually results from (a) gangrene and infection in the extremities, (b) coronary occlusion, or other complications of arteriosclerosis, (c) involvement of the renal artery orifice by the thrombus, with resultant hypertension, or uremia.

The ideal treatment would be to resect the thrombosed area and restore the circulation by bridging the arterial defect with a graft. Unfortunately, this is rarely

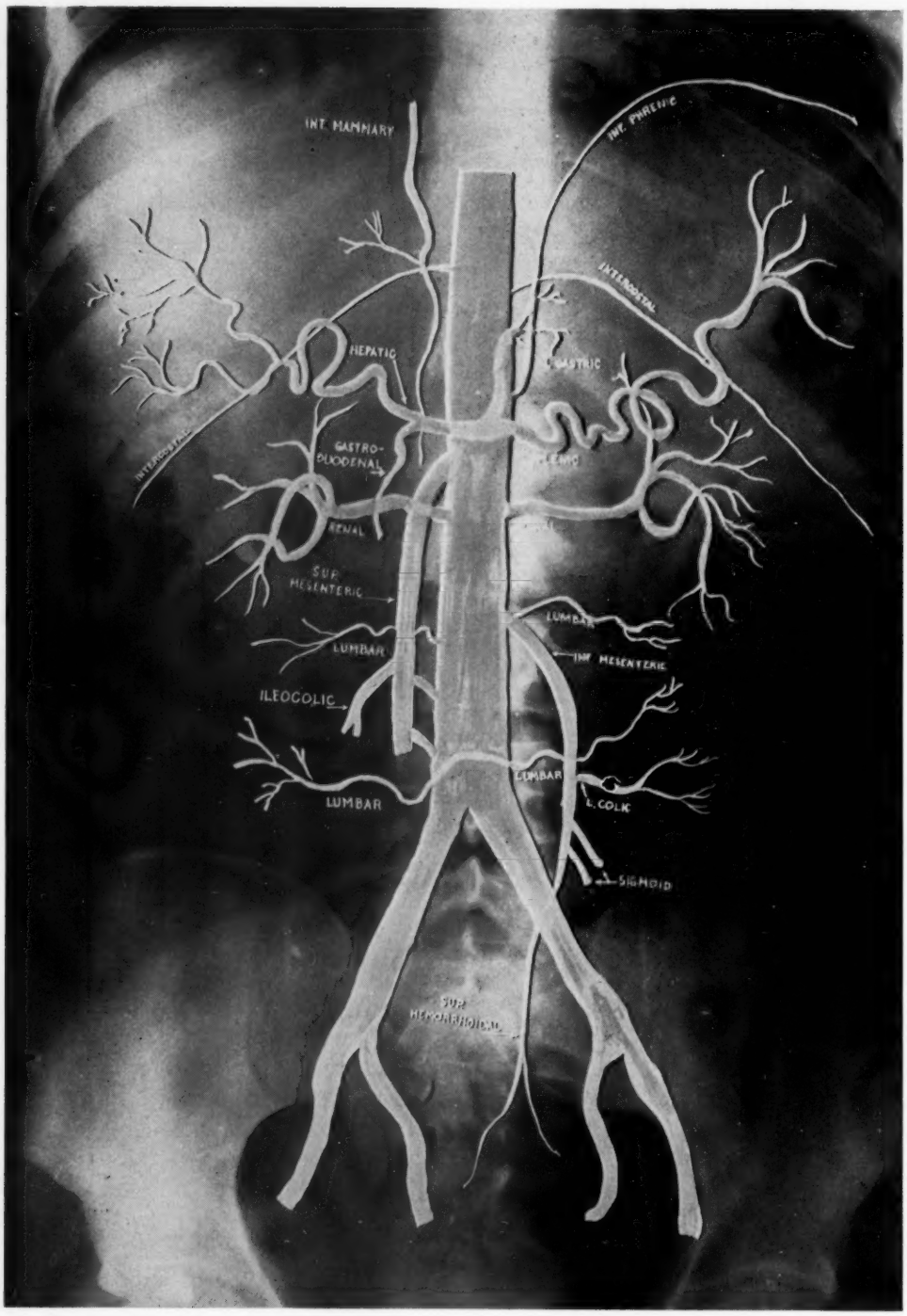


FIG. 3. Composite drawing of normal abdominal aortograms.

possible because of limitations of present surgical techniques. For lack of the ideal treatment, what remains is to improve the circulation to the lower extremities by removing the vasoconstricting nerve supply to the collateral circulation. This can be accomplished by a bilateral lumbar sympathectomy. Leriche now recommends that, when feasible, resection of the thrombosed aorta and iliac vessels be combined with

Fig. 4. Case 1. There is segmental narrowing of the proximal right common iliac artery. Note the enlarged fourth lumbar artery on the right, demonstrating the presence of collateral circulation.

sympathectomy. The resection serves a dual purpose: (a) it removes the thrombosed vessels, which may prevent the continuation of clot formation, (b) it may also remove the area of irritation, which is the site of origin of arterio-arterial vasoconstrictor reflexes to the patent collateral circulation.

## REPORT OF CASES

Case 1. H. L. D., a fifty-seven year old white male, was admitted to the Veterans Administration Hospital, Louisville, Kentucky, on December 12, 1949, because of a six months' history of moderately severe pain in the right lower extremity on exertion. This pain in the thigh and calf muscles on the right side was precipitated by walking about half a block, but after resting a moment the pain would be completely relieved, and he could then proceed another half-block. These symptoms are gradually increasing in severity. Patient also states that in the past six months he cannot maintain a stable erection.

*Physical Examination.* Blood pressure 160/92. No puslations felt in the right lower extremity, including the femoral. The pulsations in the left lower extremity appear normal. These findings were confirmed on oscillometric studies. There was slight decrease in the circumference of the right thigh, as compared with the left.

*Laboratory Findings.* Kahn reaction negative. Roentgenogram of the lumbar spine revealed spondylolisthesis of the fifth lumbar segment. There were no other abnormal findings.

*Abdominal aortogram* (Fig. 4) was done on March 21, 1950, and revealed a segment of marked narrowing of the right common iliac artery, 2 cm. distal to the aortic bifurcation. We believe this finding demonstrates the earliest roentgen manifestation of the Leriche syndrome. There was also definite enlargement of the fourth lumbar artery on the right, which demonstrates the presence of collateral circulation.

On May 22, 1950, the aorta and iliac arteries were explored by Dr. Joseph E. Hamilton. The right common iliac artery showed no pulsation, and its proximal 8 cm. was concentrically thickened; it felt as if it were partially calcified. Two centimeters distal to the aortic bifurcation the diameter of the right common iliac artery narrowed down to about 5 mm. The terminal 3 cm. of the aorta, and the proximal 5 cm. of the left common iliac artery, also showed thickening with hard calcific areas, but less marked than those in the right common iliac artery. Because of these findings, the plan of segmental excision, or venous graft, was given up. A right lumbar ganglionectomy was then performed.

*Hospital Progress.* On the third postoperative day the second toe of the left foot became violaceous in appearance, and quite painful. These symptoms in the left toe became progressively worse, and so a left lumbar sympathetic ganglionectomy was done on June 9, 1950, by Dr. Clarence E. Claugus.

The patient has had excellent response to the bilateral lumbar sympathectomy. At the time of discharge (June 19, 1950) he was able to walk about four blocks without any difficulty. The patient was instructed to return to the Vascular Follow-up Clinic.

Case II. R. K. F., a sixty-two year old white farmer, was admitted to the Norton Memorial Infirmary, Louisville, Kentucky, on November 1, 1949, because of a two year history of aching and cramp-like pain in the left leg and thigh when walking. The pain was absent during rest, but would appear after walking a few yards, usually in the region of the knee, and with continued walking up to 30 to 50 yards the pain radiated upward and downward, be-

FIG. 5. Case II. Complete absence of filling of the left common iliac artery, with narrowing of the proximal portion of the right common iliac artery. There is also some involvement of the terminal aorta. Note the collateral circulation on the left side.

coming increasingly severe. Three months ago similar symptoms appeared in the right thigh and knee, but to a lesser degree. The patient was not impotent, and could maintain a stable erection. Five years prior to admission he had a coronary artery occlusion, from which he made a good recovery.

Physical examination showed that no arterial pulsations, including the femoral, could be elicited on the left. On the right the pulsations, although diminished, were felt. After walking at a normal speed approximately 30 yards, the patient was forced to stop because of severe pain in the left thigh and calf. In the recumbent position, both feet were pallid. On dependency, the right foot slowly became pink, but the pallor on the left persisted. There appeared to be slight muscular atrophy of both calves and thighs. Blood pressure was 160/76.

Laboratory findings were all within normal limits, except for elevation of the blood cholesterol to 320 mg. per cent. The Kahn reaction was negative.

*Abdominal aortogram* (Fig. 5) revealed good filling of the aorta, and outlined several calcific plaques in the aortic wall. There was complete absence of filling of the left common iliac artery, and a narrowing of the lumen of the proximal portion of the right common iliac artery. There also appears to be some narrowing of the terminal 2 cm. of the abdominal aorta. The inferior mesenteric artery is well visualized. There is evidence of a collateral circulation on the left.

On November 10, 1949, the aortic and iliac arteries were explored by Dr. Alvin B. Ortner. The left common iliac, external iliac and internal iliac were hard, cord-like and pulseless. The aortic wall at the bifurcation was thickened. Pulsation was present in the aorta and right iliac artery. The left common iliac and proximal portion of the internal and external iliac arteries were resected. These vessels were somewhat adherent to the surrounding structures, suggesting a periarteritis, but the adhesions were not dense and dissection was not difficult. A left sympathetic ganglionectomy was combined with this procedure.

*Follow-up.* There was decided subjective and objective improvement in the left lower extremity. One month later he was able to walk five times as far as he had been able to do prior to his operation. For the first time in more than a year he could walk to his barn without stopping. A right lumbar ganglionectomy is planned to relieve symptoms in the right lower extremity which are due to the progression of the disease, with involvement of the right common iliac artery.

CASE III. M. E., a fifty year old white male, was admitted to the Louisville General Hospital on August 22, 1949, complaining of pain and weakness of both lower extremities. Following an episode of coronary heart disease in 1946, he began to experience bilateral leg pain on walking. The pain in his lower extremities had progressively become so severe that he was forced to quit work. He had not noticed any color changes in the skin of the extremities, but stated that his feet were always cold.

Physical examination showed no pulsations of the abdominal aorta below the umbilicus. While recumbent the lower extremities were markedly pallid, and remained so when dependent. No arterial pulsations were palpable in the lower extremities. Oscillometric readings were zero at all levels. The musculature of the lower extremities was flabby, and there appeared to be slight symmetrical atrophy. The patient was able to walk only about 20 yards. Blood pressure was 120/65.

Laboratory findings were within normal limits, including a negative blood Kahn reaction. The electrocardiogram showed low voltage and a left axis shift.

*Abdominal aortogram* (Fig. 6) revealed an abrupt obstruction to the flow of contrast medium in the aorta, just distal to the origin of the renal arteries. The inferior mesenteric artery, instead of coming off the aorta, is now seen to be a large collateral branch from the superior mesenteric artery. The left spermatic artery is visualized.

On September 8, 1949, exploration of the terminal aorta and iliac arteries was done by Dr. Alvin B. Ortner. No pulsation could be felt distal to the renal branches. Calcific plaques were felt in the aortic wall, but, on the whole, this portion of the aorta felt doughy. At the bifurcation there was an abrupt change in the character of the wall, the aortic bifurcation and both iliac arteries being hard and cord-like. Because of the high extension of the thrombus, it was impossible to transect proximal to it without interfering with the renal blood supply; hence the aorta was divided 2 cm. below the renal branches. The terminal aorta and iliacs were resected, and a left lumbar ganglionectomy was done.

Examination of the specimen, as reported by Dr. A. J. Miller, showed:

"Gross description: Specimen consists of the terminal aorta which is 60 mm. in length, the left common iliac artery, and the stumps of the left external and internal iliac arteries. On the right side there is a short stump of the right common iliac artery. The average diameter of the aorta was approximately 15 mm. and the average diameter of the left common iliac artery was 5 mm. The adventitial wall of the aorta was pink in color; there was moderate adventitial injection, the wall was pliable, but at the bifurcation were several calcium plates. The iliac arteries were pink in color with adventitial injection and felt hard and ropy. On section of the aortic wall, approximately 25 mm. above the bifurcation, the lumen was found to be completely obliterated due to a laminated, soft, friable thrombus. The thrombus was attached at three focal areas at this section. The intimal wall was thin and slightly variegated, the media was likewise thin. Section through the iliacs showed a marked hyperplasia of the intimal wall by yellow laminations with only a pinpoint lumen remaining. The media was calcified.

"Microscopy: The aorta is dilated and its lumen partially obstructed by a recent thrombus. The thrombus itself shows laminations of the fibrin and ghosts of the red blood cells. It is attached to the wall of the aorta at several focal points. In these areas

Fig. 6. Case III. There is an abrupt obstruction in the aorta, just distal to the origin of the renal arteries. The inferior mesenteric artery appears to be a large collateral branch from the superior mesenteric artery.

there are rather dense collections of lymphocytes and plasma cells. The intimal layer of the artery is markedly thickened as in an atheromatous process, and at the junction of the intima with the media there are irregular focal areas of calcification. The media is markedly thinned and between some of the elastic bundles there are streams of leukocytes. In the adventitia there is a marked infiltration of lymphocytes and plasma cells perivascularly. Cross sections of the iliac arteries show the thrombus to be more extensive and to be considerably older. In one of the iliac arteries partial recanalization of the thrombus has occurred, otherwise, the lesions in the walls of the iliacs are similar to those described for the aorta.

"Interpretation: Arteriosclerosis with thrombosis, aorta and common iliacs."

*Follow-up.* On September 26, 1949, a right lumbar sympathectomy was performed. There was subjective relief of pain, and the exercise tolerance, estimated by walking, was increased more than five times. Since discharge (October 5, 1949) the patient has been followed in Vascular Follow-up Clinic, and has continued to improve.

Case IV. W. K. T., a fifty-eight year old

FIG. 7. Case IV. Contrast medium fails to enter the aorta below the level of the disc space between the third and fourth lumbar bodies. There are two renal arteries, bilaterally. The block was due to a large mural thrombus, occluding the terminal aorta (see Fig. 8).

white male, was admitted to the Veterans Administration Hospital, Louisville, Kentucky, on June 5, 1950, complaining of weakness and pain in both lower extremities for the past six years. These symptoms have been increasing in severity until at the present time he cannot walk at all. He also states that for the past five years he has had a sensation of coldness in both feet and legs. In April, 1950, he developed several ulcerative lesions of the skin in the regions of the right ankle and the third and fourth left toes. In the past five years he has consulted many doctors, and was being treated for Buerger's disease.

*Physical Examination.* The patient appeared poorly nourished and chronically ill. He was also somewhat mentally confused. Blood pressure on the right was 160/100 and on the left 80/60. He had a large decubitus ulcer over the sacrum. There was absence of pulsations in both lower extremities. Oscillometer readings from the femorals down to the ankles were zero, bilaterally. There were no pulsations of the abdominal aorta below the umbilicus. With both extremities dependent, the skin appeared tight, shiny, and violaceous, but when raised to the vertical the skin showed extreme pallor, bilaterally. The musculature of both lower extremities was atrophic, somewhat more marked on the right. There were trophic changes in the form of ulcerative skin lesions, involving the left third and fourth toes, and the right ankle region. The temperature of the skin of both legs and feet was noticeably decreased.

*Laboratory Findings.* Kahn reaction was negative. Sedimentation rate was elevated, and urine analysis showed many white blood cells. The blood non-protein nitrogen was slightly elevated. Electrocardiogram showed changes suggestive of coronary insufficiency.

*Abdominal aortogram* (Fig. 7) was done on June 14, 1950, and showed slight aortic dilatation above the level of the disc space between the second and third lumbar vertebral bodies. Below this level the aorta rapidly narrowed, and then at the level of the disc space between the third and fourth lumbar bodies there was failure of contrast medium to enter the aorta. There were two renal arteries, bilaterally. Three silver clips are seen on the right side, from a previous lumbar sympathetic ganglionectomy. The inferior mesenteric artery and its branches are well shown. An extensive collateral circulation was not visualized.

*Hospital Progress.* Because of the ulcerative skin lesions, and severe pain in the right lower extremity, a right lumbar sympathetic ganglionectomy was done on June 7, 1950. Following this procedure, the color of the right extremity appeared improved, and the pain sensations were greatly diminished. On June 14, 1950, an abdominal aortogram was done (reported above), followed by a left lumbar sympathetic ganglionectomy. This again was followed by relief of pain in the left lower extremity, and the color appeared improved. He now had a sensation of warmth in both his extremities. However, it appears that the collateral circulation could not maintain adequate circulation to the lower extremities, in spite of the bilateral sympathectomies, which did relieve the pain. Because of gangrene, which gradually appeared in the toes and feet on both sides, a left mid-thigh amputation was done on August 3, 1950, and a right mid-thigh amputation was done on August 9, 1950. The patient's general condition remained poor; on August 15, 1950, it was noted that he developed a bluish discoloration of the left index finger. No left radial pulse could be

felt. A left stellate ganglion block was done, but there was no improvement. Some ten days later there was gangrene of all the left fingers except the thumb. The patient's general condition became slowly but progressively worse, and he died on October 16, 1950.

At autopsy the significant findings were a severe generalized arteriosclerosis and aortic

Fig. 8. Case iv. Gross picture of the aorta and its bifurcation, showing a very extensive mural thrombus, adherent to the intima. The thrombus extends into the common iliac arteries. Proximal to the mural thrombus are smaller thrombotic clots. The aorta is markedly sclerotic.

thrombosis, with occlusion, extending into both iliac arteries (Fig. 8). Microscopic examination confirmed these findings, and a section of the abdominal aorta near its bifurcation is shown in Figure 9. Other sections of the diseased areas were reported by Dr. Harold Gordon, as follows:

"The abdominal aorta, in sections taken from the thrombosed portion, is greatly thickened. There are

Fig. 9. Case iv. Photomicrograph of the abdominal aorta, near its bifurcation (medium high magnification). Inflammatory infiltrations are present about a small nerve fiber (upper left) in the thickened adventitia. Leukocytes are also present near some vasa vasorum (right, mid-field) at the junction of the media and the adventitia. In the thickened media (foreground) are groups of vacuolated "foam" cells and diffuse leukocytic infiltrations.

many irregular fissures in the media where the elastic fibers are replaced, to a large extent, by hyaline scars, plaques of calcium and nodular accumulations of cholesterol with groups of lipid-laden phagocytes at the periphery. In addition to the severe and advanced atherosclerosis, which affects chiefly the intima and the media, there are diffuse and nodular lymphoid infiltrations. These involve chiefly the media, but extend also into the thickened adventitia. Many of these infiltrations are present about the vasa vasorum. In one area the atherosclerotic process has produced a crater-like deformity in the intima. Here, in addition to necrotic debris and many clefts, is a conglomerate nodule of coagulated fibrin.

"A section of the right common iliac artery, taken at the site of the thrombus, is generally similar to the aorta. This artery also shows advanced atherosclerosis with deposits of cholesterol and with foci of active inflammation in the media. In addition, it contains a large thrombus which is undergoing organization, and is firmly adherent to the intima of the iliac artery.

"In summary, the two arteries show severe athero-

FIG. 10. Case v. This study was not entirely satisfactory as there is slight extravasation around the tip of the needle, and only a small amount of contrast medium is seen in the aorta and common iliacs. However, note the enlargement of the lumbar arteries, particularly on the right, and the collateral circulation with the fourth right lumbar artery.

sclerosis with superimposed mural thrombosis and with reactive inflammation."

CASE V. H. C., a forty-seven year old white male, was admitted to the Veterans Administration Hospital, Louisville, Kentucky, on February 27, 1948, complaining of intermittent cramping in both calves for the past five years. For the past year he has had pain in the low back, radiating down both legs. These symptoms have gradually progressed, and on admission he was able to walk only 75 to 100 steps before being forced to rest. He has been impotent for the past eight months. Five years ago he had an episode of coronary heart disease.

Physical examination revealed absence of pulsation of the aorta below the umbilicus; there was absence of arterial pulsations in both extremities, including the femorals. Oscillometric readings were zero at all levels. There was marked pallor of the skin of the legs and feet even when standing. There appeared to be slightly symmetrical atrophy of the musculature of both lower extremities. Blood pressure in the arms was 142/80. There was marked silver wire appearance of the arteries of the fundus.

Laboratory findings were all within normal limits.

*Abdominal Aortogram* (Fig. 10) was done on April 2, 1948. This study was not entirely satisfactory as there was difficulty in getting the needle into the aorta, and there was also slight extravasation around the tip of the needle. Only a small amount of contrast medium is seen in the aorta and common iliac arteries. However, the feature of this study was the enlargement of the lumbar arteries, particularly on the right. The fourth right lumbar artery showed extensive collateral circulation, probably with the deep circumflex iliac artery on the right.

A lumbar sympathetic block was done and there was no change in the temperature or oscillometric readings on the right, but improvement on the left. Accordingly, on April 16, 1948, a left lumbar ganglionectomy was performed by Dr. Joseph E. Hamilton. The aorta was explored and found to be surrounded by fibrous tissue, and was somewhat adherent to adjacent structures. There were no pulsations in the distal 2 cm. of the aorta, nor in the common iliac arteries. The distal aorta and common iliacs were reduced in caliber to about 6 mm.

*Follow-up.* The day following the operation the patient had his first erection in a period of eight months, and on the tenth postoperative day, while on leave from the hospital, the patient had sexual intercourse for the first time in nine months. His exercise tolerance increased. A right lumbar sympathectomy was advised, but the patient refused.

Twenty months after his left lumbar ganglionectomy he could now walk 300 to 400 steps before cramping and weakness would come on.

CASE VI. R. L. V., a sixty-three year old white carpenter, was admitted to the Veterans Administration Hospital, Louisville, Kentucky, on October 23, 1950, because of a two and one-half year history of aching and cramp-like pains in the left calf after walking. For the past year he has had pains in the left thigh, calf and leg, with extreme weariness after walking about a block. In the past six months he has developed similar pain in the right leg, although not as severe as in the left. Eight

months ago he noticed he had become impotent. He has also complained of his feet being cold, worse on the left than on the right side.

His past history is not remarkable; there is no history of coronary artery disease.

*Physical Examination.* There was absence of arterial pulsations, including the femoral on the left side. On the right there were also no pulsations, except in the femoral artery. At rest, in a supine position, the patient's lower extremities were a whitish pink in color. On elevation of the lower extremities for two minutes, the color did not change. However, with the lower extremities in a dependent position for two minutes, both feet showed mild erythema, more marked on the left than on the right. There appeared to be slight muscular atrophy of both lower extremities, more marked on the left than on the right. There were no trophic changes of the skin or toenails in either extremity. Blood pressure was 180/102.

*Laboratory Findings.* The electrocardiogram was normal. Wassermann reaction was negative. All other studies were within normal limits.

*Abdominal aortogram* (Fig. 11) was performed on October 24, 1950, and shows a slight irregular tortuosity of the terminal 9 cm. of the aorta. The aortic bifurcation is well visualized, and appears normal. Three centimeters distal to the aortic bifurcation the left common iliac artery shows an abrupt narrowing of its lumen down to 3 mm. The right common iliac artery is normal in caliber, but 0.5 cm. distal to the aortic bifurcation there is an irregular filling defect, 1 cm. in length, on the medial side of its lumen. The inferior mesenteric artery is well visualized. There is evidence of collateral circulation on the right and left sides.

*Course in Hospital.* On October 26, 1950, the patient had a lumbar sympathetic block on the left, and it was found that his left leg became warmer, and his exercise tolerance on the left increased from 825 to 1,305 feet. On November 13, 1950, a left lumbar sympathetic ganglionectomy and exploration of the terminal aorta and common iliac arteries were done by Dr. Joseph E. Hamilton. The aorta felt relatively normal to palpation down to the bifurcation, and showed good pulsation. The right iliac artery showed distinct pulsation, but it felt as if it were encircled with calcification. The left iliac artery showed pulsation for the proximal 1 cm., but it was quite faint. Distal to this, no pulsation was felt, and 3 cm. from the aortic bifurcation there was a constriction in this vessel, below which there was again palpated extensive calcification. The terminal aorta and common iliacs were adherent to the surrounding structures, suggesting a periarteritis, and, on baring and cleaning these vessels, there was some bleeding and considerable oozing. It was felt that an excision and vein graft, to bridge the defect in the left common iliac artery, was impossible because of the sclerotic changes in the vessels. The postoperative condition thus far has been satisfactory, but it is too early to evaluate the results.

Fig. 11. Case VI. There is segmental narrowing of the left common iliac artery and early involvement of the medial side of the proximal right common iliac artery.

## SUMMARY

1. A review of the literature reveals that the Leriche syndrome is rarely reported, but it is believed that the incidence of this disease is much higher than is generally appreciated.

2. The etiology and pathology of chronic thrombotic obliteration of the aortic bifurcation have been discussed.

3. The diagnostic criteria have been presented and correlated with the roentgen findings.

4. The technique of abdominal aortography has been briefly reviewed, and the value of abdominal aortography in the Leriche syndrome has been stressed.

5. Six cases of the Leriche syndrome, with typical histories, clinical findings, operative reports, and abdominal aortograms, have been presented.

6. The prognosis and treatment have been briefly discussed.

Grateful acknowledgment is made to Dr. J. C. Bell and Dr. Harold Gordon, for their criticism and advice; to Dr. A. B. Ortner and Dr. J. E. Hamilton, for the free use of their clinical material.

## ADDENDUM

During the course of preparation of this paper, 3 additional cases of chronic occlusion of the aortic bifurcation have come to our attention, with typical findings on abdominal aortograms. However, these cases have not yet been operated upon.

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# THE ROENTGEN FINDINGS IN ATELECTASIS OF THE NEWBORN

## WITH SPECIAL REFERENCE TO CHANGES IN THE CARDIAC SILHOUETTE*

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THE diagnosis of pulmonary atelectasis in the newborn is greatly dependent upon the roentgen examination of the chest, and roentgenologic studies are imperative when this condition is suspected. Clinically, inadequate initial expansion of the alveoli, or a delay in this process, may be accompanied by marked respiratory difficulty, cyanosis, tachycardia, and signs of collapse. The respiratory rate is rapid and there is diminished expansion of the thorax during inspiration with intercostal, suprasternal and substernal retraction. Cyanosis, which is a prominent feature of the disease, may be present at birth, or may become evident within a few hours.

The roentgenographic examination of the chest demonstrates clearly the extent and character of the changes in the lungs and the thorax. These findings are primarily concerned with: (1) abnormal densities in the lungs; (2) the position of the diaphragm; (3) a shift of the mediastinum; (4) narrowing or asymmetry of the intercostal spaces; (5) enlargement of the cardiac silhouette. The changes in the cardiac silhouette will receive special attention in this presentation.

The expansion of the lungs at birth is initiated by a vigorous inspiratory effort and cry, at which time sufficient alveoli are inflated to care for the physiologic needs of the infant. The expansion of the remaining alveoli is a gradual process, requiring two to six days in the full-term infant, and as long as six weeks in the premature infant.[3] This process of gradual expansion has been termed "physiologic atelectasis," and the chest roentgenogram during this period may reveal a few fine mottled densities throughout both lungs which clear within a few days.

Wilson and Farber[10] list the following factors in preventing the normal initial expansion of the lungs:

1. Cohesion of the moist surfaces of the air passages in collapsed and airless lungs.
2. Ineffective action of, or an imperfectly developed, respiratory center.
3. Underdevelopment of the bony thorax.
4. Obstruction in the bronchial tree.
5. Incomplete development of the alveoli.

Atelectasis may be either congenital or acquired. Wilson and Farber[10] divide congenital atelectasis into two groups. The first is the initial type composed of mature alveoli which have never contained air, and the second is the atelectasis of prematurity in which the lung is composed of varying amounts of immature alveoli and pulmonary tissue. The acquired form is almost always due to bronchial occlusion with absorption of air distal to the point of obstruction and is referred to as the resorption type. Caffey[2] further classifies congenital atelectasis into massive, regional, and disseminated types, according to the extent and distribution of the involvement. A combination of two or more types is commonly observed. The distribution may include an entire lung, a lobe of the lung, or a segment of a lobe, but more commonly portions of several lobes are involved.

### LUNG DENSITIES

The findings in the roentgenograms range from extensive, homogeneous opacities to disseminated, finely mottled areas of in-

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creased density. The larger homogeneous densities are more likely to be found in the premature infant and are probably associated, in some degree, with incomplete development of the alveoli. They vary in size and may be so extensive as to suggest that an entire lung is atelectatic. The branches of the air-containing bronchi may be quite prominent and easily identified in the unexpanded lung. The disseminated areas of atelectasis may appear as fine, discrete, mottled opacities measuring 1 or 2 millimeters, or as larger, irregular, poorly marginated densities as great as 5 mm. in diameter. The entire lung may be quite hazy in appearance when there is extensive involvement.

A contradictory finding in these cases of atelectasis is the occasional presence of emphysema in the basal and peripheral portions of the lungs. We are not certain whether this represents the obstructive or compensatory type. The location and appearance of the emphysema suggests that it may be the result of excessive diaphragmatic contraction in an attempt to provide further aeration of the atelectatic lung. The lung markings in these areas are diminished, resulting in increased radiolucence and providing a marked contrast to the densities in the lung. The emphysema diminishes with increasing expansion of the atelectatic lung.

The interval required for complete expansion of the lungs in the cyanotic newborn varies from a few days to a few weeks and is partially related to the stage of development of the alveoli. The cyanotic premature infant may require as long as six weeks for complete expansion while a full-term infant may require only a few days.

Partial or complete obliteration of the sharp cardiac margins usually found in the chest roentgenogram of the newborn was one of the most important and most consistent findings in these cases of atelectasis. This was due to the projection of atelectatic lung upon the cardiac silhouette. All of the cases presented this feature. In some instances, the involvement was so extensive as to completely obliterate the cardiac margin, making it impossible to measure the transverse diameter of the heart. They become more sharply defined as the lung overlying and surrounding the cardiac silhouette becomes aerated. This finding may serve as an important aid in differentiating between atelectasis and congenital heart disease in the newborn. Both may be present in the newborn, but we cannot evaluate the contour of the cardiac silhouette until the atelectasis has cleared sufficiently so as to exclude the influence of anoxia, tachycardia and intrathoracic volume changes in the lung.

### MEDIASTINUM

The mediastinum in the normal newborn infant is wider than later in life. The changes described by Noback[7] in his anatomical study of the thymus gland are well demonstrated by the chest roentgenograms. He believes the molding of the thymus gland bears a direct relationship to the establishment of respiration and is dependent upon the expansion of the lungs. The thymus in the liveborn was elongated and molded so that the anterior, lateral and posterior surfaces bore impressions of all of the organs with which it was in contact. The thymus was the broad, or fetal, type in infants who had never breathed. A gradual decrease in the width of the mediastinum is observed as the pressure of the expanding lungs gradually molds the thymus gland. This is observed to some degree in normal infants, but becomes more prominent in those who are cyanotic at birth.

Shift of the mediastinum is not always observed in congential atelectasis because of the common bilateral distribution, and this is especially true in the disseminated type where the atelectasis is distributed diffusely throughout both lungs. Under these conditions, the decreased volume of one lung may not be great enough to cause a sufficient pressure differential between the two lungs to shift the mediastinum. Mediastinal shift does occur when there is marked involvement of one lung.

### DIAPHRAGM

The diaphragm of the newborn infant is probably the most important muscle of respiration in this period of life and is characterized by a smooth curvilinear contour in the chest roentgenogram. It is elevated in the resorption type[5] of atelectasis, partially compensating for the decreased volume of the lung, but the smooth contour is usually maintained. The diaphragm is elevated in congenital atelectasis when there is a severe degree of involvement of one lung. This occurs in both the massive and disseminated types. With increasing aeration of the lung, it may become irregular and flattened. This is due to the increased effort and stress of the component parts in attempting to expand the remaining atelectatic lung. In some cases, the diaphragm is identified by incomplete and irregular lines of horizontal density, while in others the sharp definition is maintained but the contour is flattened. The flattening is accompanied by emphysema which has developed in the basal and peripheral portions of the lung. The diaphragm assumes a normal contour as the atelectatic lung expands and the intrathoracic pressure returns to normal.

### INTERCOSTAL SPACES

In the cases described here, the intrathoracic volume deficit of the lung resulted in varying degrees of narrowing of the intercostal spaces and other deformities of the bony thorax. This was present primarily in those cases with a severe degree of atelectasis of one lung. The narrowing of the intercostal spaces was not a constant feature in the disseminated type, even though a severe degree of atelectasis was present. This is probably due to the presence of emphysema in the peripheral portions of the lung which partially reduces the intrathoracic volume deficit. In those cases in which the muscle tone is maintained, the changes consist of slight narrowing and asymmetry of the intercostal spaces. The deformities of the thorax are more marked when the muscle tone is poor or absent. In such instances, the thorax may show normal anatomic relationships in one portion, while the remaining intercostal spaces are markedly deformed and asymmetrical. The extent of the thoracic deformity is dependent upon the degree of spinal cord, brain and muscle involvement. This emphasizes the importance of a stable bony thorax in aiding expansion of the lungs, as pointed out by Wilson and Farber.[10] All of the patients, except those with disseminated atelectasis, show some detectable degree of asymmetry or deformity of the bony thorax. In one infant with extensive spinal cord damage, the upper half of the thorax was partially collapsed, while in the lower half the intercostal spacings were normal.

### CARDIAC CHANGES

Enlargement of the cardiac silhouette in the new born is usually considered to represent an organic abnormality of the heart. This includes developmental anomalies of many types, as well as cardiac musculature abnormalities such as idiopathic hypertrophy of the heart, glycogen storage disease, and rhabdomyoma. Recently, our attention has been directed to a group of cases in which the cardiac enlargement, as evidenced by the roentgenogram, is secondary to atelectasis rather than to congenital heart disease.

Farrell[4] studied the chest roentgenogram in the newborn infant in 159 cases with films taken within forty-eight hours after birth, within ten days, and in several cases within the six month period. The mean width of the bony thorax in inspiration was found to be 9 cm. in males, and 8.9 cm. in females. The mean transverse diameter of the heart was 5.0 cm. in both males and females. The cardiothoracic ratio was 0.55. Bakwin and Bakwin[1] studied the chest in 52 newborn infants and found a mean cardiothoracic ratio of 0.55 (standard deviation = 0.049) in the first three weeks of life. In their series, the mean transverse diameter of the heart was 49 mm. (std. dev. = 6 mm.). The mean length of the

TABLE I

THORACIC MEASUREMENTS IN NORMAL FULL-TERM NEWBORN INFANTS

| Case No. | Birth Weight in Grams | Transverse Diameter of Heart (in cm.) Age in Days | | | Transverse Diameter of Thorax (in cm.) Age in Days | | | Cardiothoracic ratio (%) Age in Days | | | Length of Thorax (in cm.) Age in Days | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 3 | 5 | 1 | 3 | 5 | 1 | 3 | 5 | 1 | 3 | 5 |
| 1 | 3,390 | 5.1 | 5.0 | 5.0 | 9.1 | 9.0 | 9.5 | .56 | .56 | .53 | 5.5 | 5.3 | 5.5 |
| 2 | 2,710 | 5.4 | 4.3 | 4.3 | 8.0 | 7.9 | 8.1 | .55 | .54 | .53 | 4.8 | 4.7 | 5.3 |
| 3 | 2,960 | 4.6 | 4.6 | 4.5 | 7.8 | 8.9 | 8.4 | .59 | .52 | .54 | 3.6 | 5.2 | 5.3 |
| 4 | 2,580 | 4.6 | 4.4 | 4.5 | 8.2 | 8.6 | 8.5 | .56 | .51 | .53 | 4.0 | 4.2 | 3.9 |
| 5 | 2,840 | 5.1 | 5.0 | 5.1 | 9.0 | 9.2 | 9.1 | .57 | .54 | .56 | 4.9 | 5.2 | 5.2 |
| 6 | 3,790 | 5.4 | 5.0 | 5.0 | 9.4 | 9.3 | 9.0 | .57 | .54 | .56 | 5.2 | 5.7 | 5.0 |
| 7 | 3,450 | 4.8 | 4.8 | 5.0 | 9.2 | 9.7 | 9.5 | .52 | .49 | .53 | 4.8 | 4.6 | 4.8 |
| 8 | 2,920 | 4.6 | 4.6 | 4.5 | 8.4 | 9.3 | 9.3 | .55 | .49 | .48 | 5.0 | 5.2 | 4.8 |
| 9 | 2,980 | 5.0 | 4.5 | 5.1 | 8.3 | 8.8 | 9.0 | .60 | .51 | .57 | 3.9 | 4.7 | 5.3 |
| 10 | 3,680 | 4.7 | 4.5 | 4.6 | 9.4 | 9.6 | 9.4 | .50 | .47 | .49 | 5.5 | 5.8 | 5.6 |
| 11 | 3,200 | 5.4 | 5.1 | 5.3 | 9.5 | 9.8 | 9.7 | .57 | .52 | .55 | 5.1 | 5.5 | 5.1 |
| 12 | 3,050 | 5.0 | 5.1 | 4.8 | 9.0 | 8.7 | 8.7 | .56 | .59 | .55 | 4.6 | 5.1 | 4.9 |
| 13 | 4,650 | 5.8 | 5.4 | 4.8 | 10.0 | 10.4 | 9.2 | .58 | .52 | .52 | 6.0 | 6.0 | 5.8 |
| 14 | 2,950 | 5.0 | 4.9 | 4.6 | 8.6 | 9.0 | 8.8 | .58 | .53 | .52 | 4.3 | 4.8 | 4.5 |
| 15 | 5,046 | 5.8 | 5.5 | 5.4 | 10.1 | 10.4 | 10.7 | .57 | .53 | .50 | 5.4 | 5.8 | 5.7 |
| 16 | 3,030 | 4.6 | 4.6 | 4.0 | 8.6 | 8.8 | 8.8 | .53 | .52 | .45 | 5.3 | 4.6 | 5.8 |
| 17 | 3,190 | 4.8 | 4.8 | | 9.6 | 9.5 | | .50 | .51 | | 5.2 | 5.2 | |
| 18 | 3,720 | 5.5 | 5.1 | | 8.9 | 9.2 | | .62 | .55 | | 4.5 | 5.2 | |
| 19 | 2,930 | 4.5 | 4.2 | | 9.2 | 8.9 | | .49 | .47 | | 4.8 | 4.7 | |
| 20 | 3,580 | 5.1 | 5.0 | | 9.3 | 9.6 | | .55 | .52 | | 5.2 | 5.8 | |
| 21 | 3,000 | 5.3 | 5.0 | | 9.7 | 9.6 | | .55 | .52 | | 4.7 | 5.5 | |
| 22 | 3,020 | 4.3 | 4.0 | | 8.9 | 9.1 | | .48 | .44 | | 4.5 | 5.1 | |
| 23 | 3,560 | 5.2 | 5.3 | | 9.0 | 9.4 | | .58 | .56 | | 5.2 | 5.3 | |
| 24 | 4,140 | 5.8 | 5.5 | | 9.3 | 9.6 | | .62 | .57 | | 4.3 | 4.8 | |
| 25 | 2,600 | 4.7 | 4.3 | | 8.1 | 8.4 | | .58 | .51 | | 4.9 | 5.3 | |
| 26 | 3,420 | 5.3 | 5.0 | | 8.7 | 8.9 | | .61 | .56 | | 4.7 | 5.2 | |
| 27 | 3,580 | 4.6 | 4.6 | | 8.8 | 9.2 | | .52 | .50 | | 5.0 | 5.2 | |
| 28 | 3,420 | 5.7 | 5.4 | | 9.3 | 9.1 | | .61 | .59 | | 4.5 | 4.6 | |
| 29 | 3,000 | 5.1 | 5.2 | | 9.6 | 9.7 | | .53 | .54 | | 5.6 | 6.1 | |
| 30 | 3,400 | 5.0 | 5.0 | | 9.2 | 9.9 | | .54 | .51 | | 5.0 | 5.3 | |
| 31 | 3,140 | 4.7 | 4.9 | | 9.2 | 8.9 | | .51 | .55 | | 4.0 | 4.6 | |
| 32 | 3,200 | 5.0 | 4.9 | | 9.5 | 9.8 | | .53 | .50 | | 4.5 | 4.9 | |
| 33 | 4,150 | 5.3 | 5.0 | | 9.3 | 9.2 | | .57 | .54 | | 4.4 | 4.4 | |
| | Mean | 5.02 | 4.86 | 4.78 | 9.04 | 9.25 | 9.11 | .556 | .525 | .526 | 4.82 | 5.14 | 5.16 |
| | Standard Deviation | .41 | .37 | .37 | .55 | .52 | .59 | .037 | .033 | .031 | .53 | .47 | .49 |

thorax was 51 mm. (std. dev. = 8 mm.) and the mean width of the thorax was 90 mm. (std. dev. = 8 mm.) In their study, the roentgenograms were made in the anteroposterior projection at a target-film distance of 2 meters, and no attempt was made at timing according to the phase of respiration. They believe the relatively large transverse diameter of the heart in infancy is due to its transverse position. They estimate that if the heart, which lies at the angle of 32 degrees in the thorax of the newborn infant, were tilted up to the angle in the average adult (45°), the transverse diameter of the heart would be shortened from 49.7 to 41.4 mm., and the cardiothoracic ratio would be 0.46, approximating the ratio found in adults, which varies from 0.40 to 0.50. Their cases, however, were not tabulated and do not permit an evaluation of the changes that may occur in the first week of life.

TABLE II

THORACIC MEASUREMENTS IN FULL-TERM NEWBORN INFANTS WHO WERE CYANOTIC AT BIRTH

| Case No. | Birth Weight in Grams | Transverse Diameter of Heart (in cm.) Age in Days | | | Transverse Diameter of Thorax (in cm.) Age in Days | | | Cardiothoracic Ratio (%) Age in Days | | | Length of Thorax (in cm.) Age in Days | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 3–6 | 7–13 | 1 | 3–6 | 7–13 | 1 | 3–6 | 7–13 | 1 | 3–6 | 7–13 |
| 1 | 3,765 | 6.0 | 5.8 | 5.6 | 9.1 | 9.7 | 9.5 | .66 | .60 | .59 | 4.6 | 4.6 | 5.0 |
| 2 | 3,920 | 5.5 | 5.4 | 5.0 | 9.2 | 9.1 | 9.2 | .60 | .59 | .54 | 5.4 | 5.7 | 6.2 |
| 3 | 2,700 | 5.9 | 5.5 | 5.0 | 10.3 | 9.1 | 9.9 | .57 | .60 | .51 | 4.7 | 3.4 | 4.6 |
| 4 | 2,810 | 5.5 | | 4.7 | 9.4 | | 9.2 | .59 | | .51 | 5.0 | | 4.8 |
| 5 | 2,925 | 5.0 | | 4.8 | 8.2 | | 9.4 | .61 | | .51 | 4.8 | | 5.1 |
| 6 | 2,630 | 5.4 | | 4.8 | 8.7 | | 9.1 | .62 | | .53 | 4.1 | | 4.8 |
| 7 | 2,950 | 5.4 | | 5.0 | 8.8 | | 9.1 | .61 | | .55 | 5.2 | | 5.5 |
| 8 | 3,500 | 6.7 | | | 10.2 | | | .66 | | | 5.5 | | |
| 9 | 2,825 | | 4.0 | 4.0 | | 7.0 | 7.2 | | .57 | .56 | | 4.1 | 4.1 |
| 10 | 2,982 | 6.0 | 5.4 | 4.7 | 8.8 | 8.6 | 8.5 | .68 | .63 | .55 | 4.4 | 3.8 | 4.7 |
| 11 | 2,850 | 5.7 | | | 8.5 | | | .67 | | | 4.6 | | |
| 12 | 3,650 | 6.5 | | | 10.1 | | | .64 | | | 4.8 | | |
| 13 | 3,300 | 5.5 | 5.5 | | 8.6 | 9.5 | | .64 | .58 | | 4.7 | 5.5 | |
| 14 | 4,700 | 6.5 | 5.3 | | 9.8 | 9.8 | | .66 | .54 | | 4.7 | 4.9 | |
| 15 | 3,560 | 5.7 | 4.8 | | 8.3 | 8.3 | | .69 | .58 | | 4.9 | 5.5 | |
| 16 | 3,380 | 5.4 | 4.9 | | 9.0 | 9.3 | | .60 | .53 | | 4.9 | 5.5 | |
| 17 | 3,710 | 5.7 | 5.1 | | 8.8 | 9.5 | | .65 | .54 | | 4.1 | 5.2 | |
| 18 | 3,990 | 5.6 | 5.6 | | 8.9 | 8.8 | | .63 | .64 | | 4.3 | 4.5 | |
| 19 | 3,420 | 6.1 | 5.4 | | 9.6 | 10.0 | | .64 | .54 | | 4.7 | 5.1 | |
| | Mean | 5.78 | 5.23 | 4.84 | 9.13 | 9.06 | 9.01 | .634 | .578 | .539 | 4.74 | 4.82 | 4.98 |
| Standard Deviation | | .44 | .46 | .39 | .62 | .79 | .73 | .032 | .035 | .026 | .37 | .71 | .56 |

TABLE III

COMPARISON OF MEASUREMENTS IN CHEST ROENTGENOGRAMS IN FULL-TERM INFANTS

| Author | No. of Cases | Age of Infant | Mean (cm.) Transverse Diameter of Heart | Mean (cm.) Transverse Diameter of Thorax | Mean (%) Cardiothoracic Ratio | Mean (cm.) Length of Thorax |
|---|---|---|---|---|---|---|
| Farrell[4] Normal | 159 | to 48 hr. | 5.0 | 9.0 | .55 | |
| Bakwin and Bakwin[1] Normal | 14 | Birth | 4.9±6 mm.* | 9.0±8 mm. | .55±.049 | 5.1±8 mm. |
| | 18 | 1 mo. | 5.4 | 9.5 | | 5.5 |
| Normal | 33 | 1 day | 5.02±.41 | 9.04±.55 | .556±.037 | 4.82±.53 |
| | 33 | 3 days | 4.86±.37 | 9.25±.52 | .525±.033 | 5.14±.47 |
| | 17 | 5 days | 4.78±.37 | 9.11±.59 | .526±.031 | 5.16±.49 |
| Cyanotic | 18 | 1 day | 5.78±.44 | 9.13±.62 | .634±.032 | 4.74±.37 |
| | 12 | 4– 6 days | 5.23±.46 | 9.06±.79 | .578±.035 | 4.82±.71 |
| | 9 | 7–13 days | 4.84±.39 | 9.01±.73 | .539±.026 | 4.98±.56 |

* Standard deviation.

TABLE IV

STATISTICAL COMPARISON OF THE CARDIAC MEASUREMENTS IN NORMAL AND IN CYANOTIC NEWBORN INFANTS

| | | Cardiothoracic Ratio | | | Transverse Diameter of Heart | | | Length of Thorax | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Mean | Critical Ratio | P | Mean | Critical Ratio | P | Mean | Critical Ratio | P |
| Normal | Day 1 | .556±.037 | 6.31 | <.0001 | 5.02±.41 | 5.15 | <.0001 | 4.82±.53 | 4.75 | <.0001 |
| Normal | Day 3 | .525±.33 | | | 4.86±.37 | | | 5.14±.47 | | |
| Normal | Day 3 | .525±.033 | .15 | .8808 | 4.86±.37 | .69 | .4902 | 5.14±.47 | .05 | .9602 |
| Normal | Day 5 | .526±.031 | | | 4.78±.37 | | | 5.16±.49 | | |
| Normal | Day 1 | .525±.037 | 7.91 | <.0001 | 5.02±.41 | 6.06 | <.0001 | 4.82±.53 | .56 | .5754 |
| Cyanotic | Day 1 | .634±.032 | | | 5.78±.44 | | | 4.74±.37 | | |
| Normal | Day 3 | .525±.033 | 4.62 | <.0001 | 4.86±.37 | 2.45 | .0142 | 5.14±.47 | 1.45 | .1470 |
| Cyanotic | Day 4–6 | .578±.035 | | | 5.23±.46 | | | 4.82±.71 | | |

P: The probability of getting, by chance alone, a difference as great as that observed. P less than .03 is statistically significant.

Critical ratio: $\frac{\text{Difference in the means}}{\text{Standard deviation of the difference of the means}}$.

Maresch and Washburn[6] presented an excellent study of the heart size in healthy children, but their series includes only 3 cases studied before the age of one month.

In order to study the change that occurs in the intrathoracic structures in the first days of life, a group of normal and a group of obviously cyanotic infants were reviewed. Thirty-three normal full-term newborn infants from the Obstetrical Service of University Hospitals of Cleveland were studied by chest roentgenograms at the age of one, three and five days. The criteria applied to the normal infant group included the following clinical findings:

1. Spontaneous cry at birth as recorded on the obstetrical anesthesia record.
2. Normal respirations in the immediate newborn period.
3. No cyanosis.
4. Minimum birth weight of 2,500 grams.
5. No maternal abnormality.
6. No fetal abnormality.

The following measurements were made on each roentgenogram:

1. The greatest transverse diameter of the heart.
2. The transverse diameter of the thorax as measured at the level of the dome of the right half of the diaphragm.
3. The length of the thorax as measured from the superior margin of the right first rib posteriorly to the dome of the right half of the diaphragm.
4. The cardiothoracic ratio was calculated for each study.

The chest roentgenograms were made in the anteroposterior projection at a 40 inch target-film distance with the infant in the recumbent position. An attempt was made to obtain roentgenograms in inspiration. Roentgenograms showing any degree of rotation, or an inadequate inspiration, were discarded.

The abnormal group included those full-term infants who were cyanotic at birth or who developed cyanosis shortly thereafter and were in obvious respiratory distress. All infants were examined by a member of the staff of Babies and Childrens Hospital. Many were admitted for further therapy. In some instances, there was evidence of damage to the central nervous system or the spinal cord.

The data obtained in the normal and cyanotic full-term newborn infant groups were analyzed statistically. The following observations were made:

A comparison of the cardiothoracic ratios in 33 normal infants examined on Day 1 and again on Day 3 reveals a very significant difference between the two groups,

indicating that a decrease in the ratio occurs normally. The comparison of the cardiothoracic ratios in 16 normal infants examined on Day 3 and again on Day 5 reveals no significant difference, indicating that the ratio at this time had reached a state of relative stability. There was a very significant difference between the cardiothoracic ratios obtained in the normal infants examined on the first day of life and the cyanotic infants on the first day of life, indicating that the ratio in the cyanotic group was significantly larger than that in the normal newborn infant group. Because there is no great difference between the cardiothoracic ratios of normal infants on Day 3 and on Day 5, we feel justified in comparing measurements made on Days 4 to 6 on the cyanotic infants with those obtained in the normal infants on Day 3. A comparison of these two groups (Normal Day 3 with Cyanotic Day 4–6) reveals a very significant difference, indicating that by the 4th to 6th day of life, the cardiothoracic ratio of the cyanotic group is not yet normal. The few cases in which a measurement was made in the cyanotic group on Days 7 to 13 gives indication that the ratio is still decreasing, but since only 5 cases are recorded, an analysis of this group is not possible at this time.

The same statements are true if a similar comparison is made using the transverse diameter of the heart in the normal and cyanotic infant groups. However, using the cardiothoracic ratio, the differences are relatively greater and therefore more significant.

A comparison of the length of the thorax in the cyanotic and normal infant groups reveals a significant increase in this measurement between the first and third days of life in the normal newborn infant. Even though the data do not show that there is a significant difference ($P=0.147$) between the length of the thorax in normal infants on Day 3 and that of the cyanotic infants of Days 4 to 6, it should be recognized that the differences may be real. The lack of statistical proof may well be due to the small size (12) of the cyanotic group.*

## REPORT OF CASES

Case I. B. G. D. The patient was a full-term newborn female infant. The pregnancy was uncomplicated and the delivery was normal. Birth weight was 2,921 grams. The physical examination revealed no abnormality. The hospital course was uneventful.

*Roentgenographic Findings.* A study (Fig. 1*A* and *B*) was made on the first day of life. The transverse diameter of the heart (TDH) was 5.0 cm., the transverse diameter of the thorax (TDT) was 8.6 cm., the cardiothoracic ratio (CTR) was 0.58 and the length of the thorax (LT) was 4.3 cm. The cardiac margins were sharply defined and a few mottled densities are present in the lungs. Figure 1*C* was taken at the age of three days. There was some slight change in the measurements. The transverse diameter of the heart was 4.8 cm., the transverse diameter of the thorax was 9.0 cm., the cardiothoracic ratio was 0.53 and the length of the thorax was 4.8 cm. Figure 1*D* was taken at the age of five days. The TDH has decreased to 4.6 cm., the CTR decreased to 0.52, the TDT was 8.8 cm., and the LT was 4.5 cm.

This case demonstrates the changes that occur in the normal newborn infant. There was a decrease in the transverse diameter of the heart and the cardiothoracic ratio. There was a slight increase in the length of the thorax and the transverse diameter of the thorax. The mediastinum decreased in width during this period. We believe that the changes in the measurements represent the increased volume of the lung secondary to the increased initial expansion that occurs during this period.

Case II. B. G. H. The patient was a full-term newborn infant, delivered after a prolonged labor in which a face presentation was changed to a vertex presentation. A few hours after birth, the patient developed fever, hemoptysis, cyanosis and a rapid respiratory rate. Birth weight was 3,500 grams. At the

* The coefficient of variation ($\sigma$/mean) of the cardiothoracic ratio for Normal Day 1 is 6.6 per cent as compared with 8.2 per cent for the transverse diameter of the hearts of normal infants on Day 1. This indicates that normals are more nearly alike when compared in this respect to the cardiothoracic ratios than when compared by the transverse diameter of the heart. A significant difference still exists if the transverse diameters of the heart are used. Using the cardiothoracic ratio, however, the differences are relatively greater and therefore more significant.

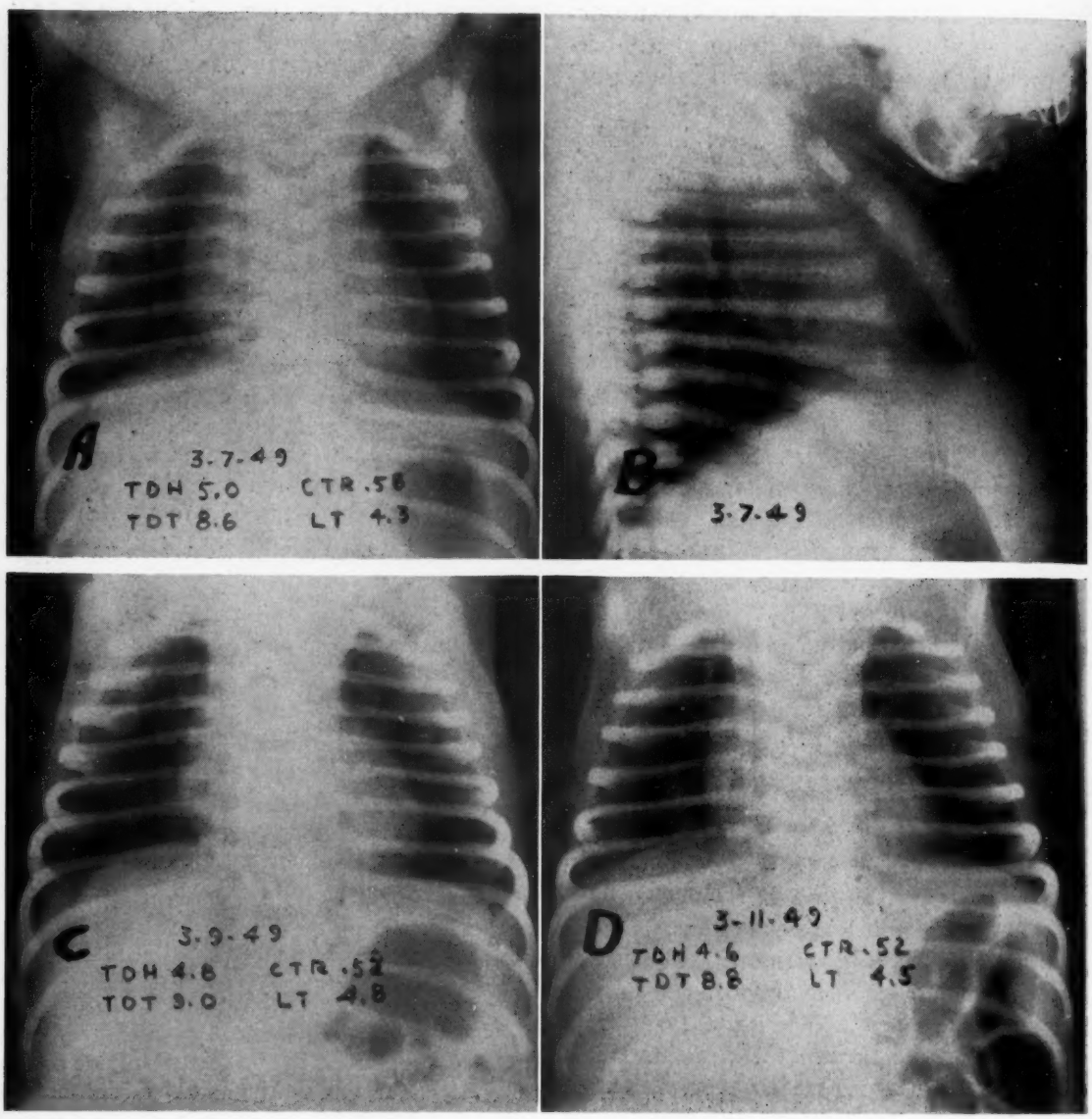


FIG. 1. Case 1. Normal newborn infant. The film studies obtained on the first, third and fifth days of life demonstrate a decrease in the transverse diameter of the heart and the cardiothoracic ratio. There was an increase in the length of the thorax. The cardiac margins are sharply defined.

physical examination, pulse was 180 and respiration 50. The infant was acutely ill and cyanotic with a weak cry. The respirations were shallow and there was retraction of the intercostal, suprasternal and infrasternal spaces in inspiration. The breath sounds were diminished throughout the chest but there was no dullness to percussion. No heart murmurs were heard.

Lumbar puncture on the second hospital day revealed xanthochromic fluid which contained 1,500 red blood cells per cu. mm. of fluid and 205 mg. per cent of protein. The pressure was low and there was evidence of a block in the spinal cord. The patient was treated with vitamin K and positive pressure oxygen and carbon dioxide. On the morning of the second hospital day, it was noted that the patient had developed a progressive complete paralysis of both arms. On the evening of the second hospital day, the paralysis had extended to involve both legs. The patient died on the fourth hospital day.

*Roentgenographic Findings* (Case 8, Table II). There are diffuse mottled densities in the medial portions of both lungs, more marked on the left (Fig. 2*A*). The peripheral and basal por-

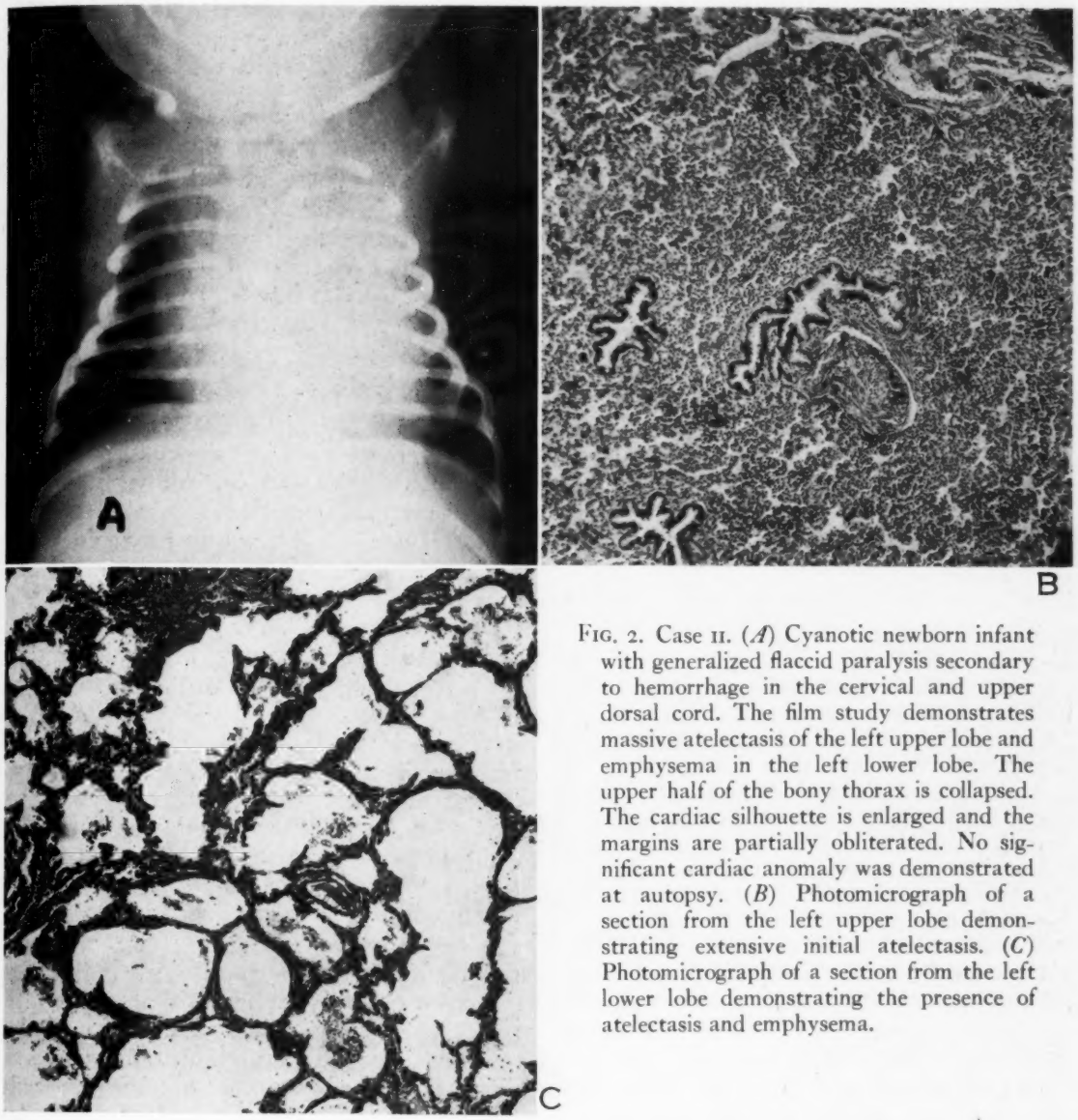


Fig. 2. Case II. (*A*) Cyanotic newborn infant with generalized flaccid paralysis secondary to hemorrhage in the cervical and upper dorsal cord. The film study demonstrates massive atelectasis of the left upper lobe and emphysema in the left lower lobe. The upper half of the bony thorax is collapsed. The cardiac silhouette is enlarged and the margins are partially obliterated. No significant cardiac anomaly was demonstrated at autopsy. (*B*) Photomicrograph of a section from the left upper lobe demonstrating extensive initial atelectasis. (*C*) Photomicrograph of a section from the left lower lobe demonstrating the presence of atelectasis and emphysema.

tions of the lungs are emphysematous. There is obliteration of the upper two-thirds of the cardiac margins. The cardiac silhouette is enlarged and the cardiothoracic ratio is 0.66. The upper six intercostal spaces are narrowed and asymmetrical bilaterally with marked deformity of the upper thorax. The upper half of the thorax is partially collapsed while in the lower half the intercostal spacings are normal. The mediastinum is shifted slightly to the right. The diaphragm is slightly flattened.

*Postmortem Examination.* Brain and spinal cord: Recent intramedullary hemorrhage of the cervical and upper thoracic spinal cord, consistent with transverse myelopathy. Lungs: Pulmonary atelectasis, moderate to marked, involving all lobes; focal complementary emphysema. Heart: Weight—28 grams; subendocardial petechiae; patent ductus arteriosus, functional; patent foramen ovale, anatomic.

Figure 2*B* is a photomicrograph of a section of the left upper lobe. There is marked atelectasis of the lobe although the general architecture is orderly. The smaller bronchi are collapsed but the epithelial lining is intact. The photomicrograph of a section of the left lower lobe (Fig. 2*C*) shows marked emphysema with thickened septa. Many spurs are present which represent the remnants of ruptured alveolar walls. In one area, atelectasis is present, while immediately adjacent there is an area of emphysema,

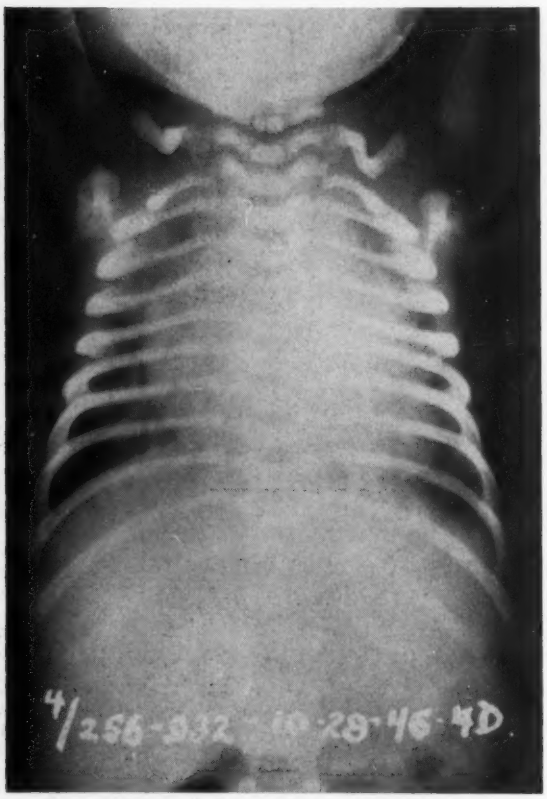

FIG. 3. Case III. Cyanotic premature newborn infant with disseminated atelectasis in the right lung. There is no shift of the mediastinum. The cardiac silhouette is enlarged. The cardiac margins are partially obliterated. No cardiac anomaly was demonstrated at autopsy.

CASE III. B. G. S. The patient was a premature infant with a weak cry. Cyanosis and respiratory distress were present at birth. Birth weight was 1,860 grams.

*Physical Examination.* There was cyanosis of the fingers, toes and ears. The respirations were rapid and regular. A few scattered petechiae were present on the chin and left cheek. The lungs were clear to physical examination. No heart murmurs were heard.

The infant was treated with oxygen with some diminution in cyanosis. On the tenth hospital day, the patient developed a mild diarrhea. The patient also had increasing jaundice. Signs of pneumonia developed and the patient died on the twenty-sixth hospital day.

*Roentgenographic Findings.* There was diffuse mottling of the medial half of both lung fields and haziness of the upper left cardiac margin. The peripheral portions of the lungs were emphysematous. The cardiothoracic ratio was 0.75. The intercostal spaces were slightly narrowed bilaterally and the diaphragm was slightly flattened.

*Postmortem Examination.* Brain: Old cerebral hemorrhage, right occipital lobe. Heart: Weight 15.5 grams; patent ductus arteriosus; patent foramen ovale, non-functional. Lungs: Atelectasis, partial, of all lobes; emphysema, slight, of all lobes; chronic passive hyperemia; focal intra-alveolar hemorrhage.

CASE IV. B. G. B. The patient was a newborn infant who was admitted to Babies and Childrens Hospital because of a weak cry and slight cyanosis. Birth weight was 2,825 grams. At physical examination the pulse was 110, respiration 68. The respirations were shallow and there was retraction of the intercostal spaces. There was dullness to percussion over the left chest and a few dry rales were heard at the left base posteriorly. The breath sounds were diminished bilaterally but to a greater degree on the right than on the left. The heart sounds were of good quality and no murmurs were heard.

The patient was given continuous oxygen with positive pressure for three to four minutes every four hours. Penicillin aerosol was given for twelve days. There was a gradual improvement in the cyanosis. The respiratory rate remained elevated for twenty-one days and then gradually returned to normal.

*Roentgenographic Findings* (Case 9, Table II). The initial roentgenographic study (Fig. 4*A*) shows massive atelectasis of the entire right lung with complete obliteration of the right cardiac margin so that the transverse diameter of the heart could not be measured. There were small areas of atelectasis in the left lung. The mediastinum is shifted to the right. The right intercostal spaces are narrowed and appear partially collapsed. The left intercostal spaces are normal in width. The right half of the diaphragm is obscured by dense lung shadow and the left is slightly flattened. A second roentgenogram (Fig. 4*B*) was made six days later. A moderate degree of expansion of the right lung has occurred although many areas of atelectasis persist. The cardiac margins are more sharply defined. The cardiothoracic ratio is 0.57. The mediastinum remains shifted to the right and the intercostal spaces have not changed. A third roentgen study (Fig. 4*C*) was made twelve days after Figure 4*A*. Further

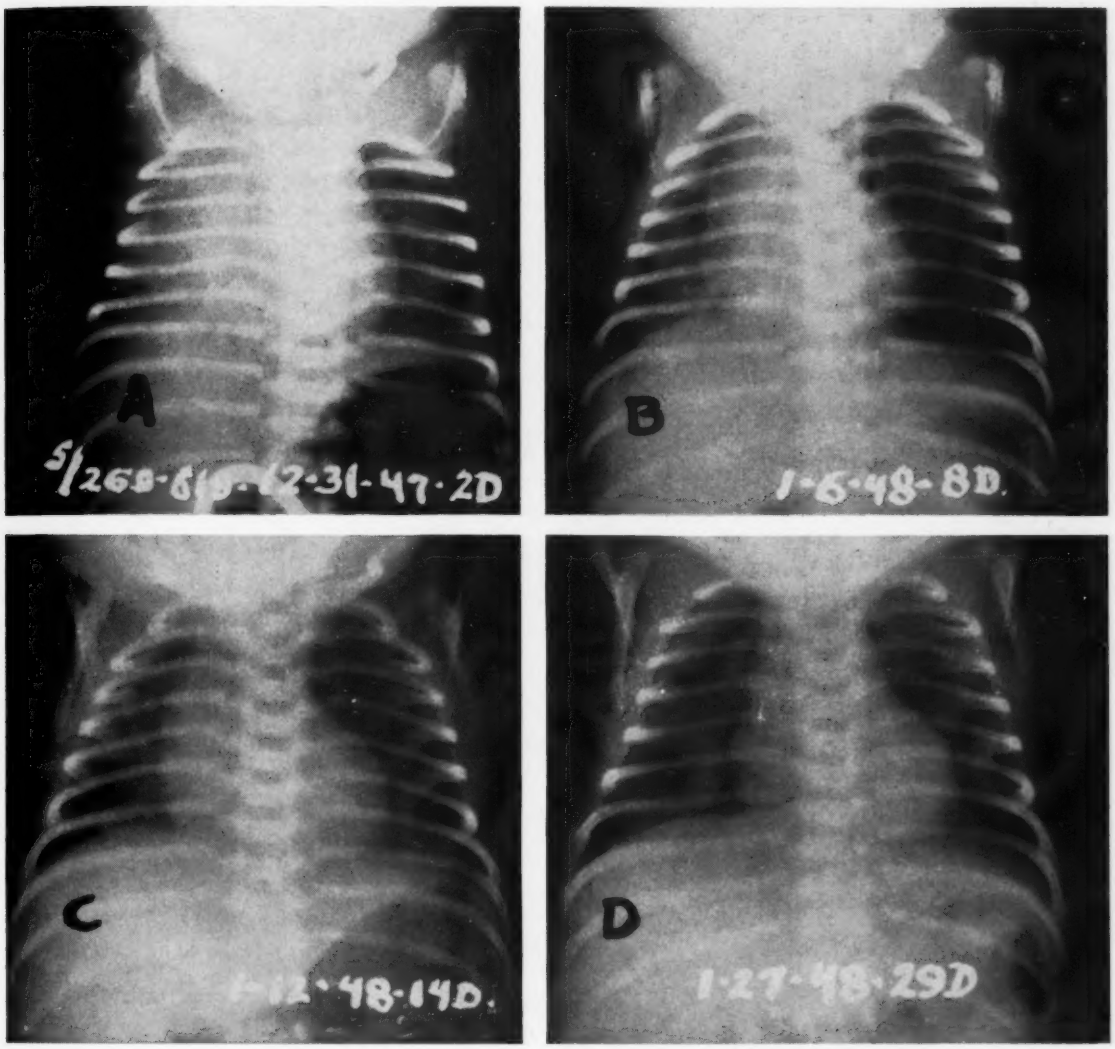


Fig. 4. Case iv. Cyanotic newborn infant with massive atelectasis in the right lung. There is a shift of the mediastinum to the right and elevation of the right leaf of the diaphragm. Approximately twenty-nine days were required for complete expansion of the lung.

expansion of the right lung has occurred but the upper right mediastinal margin is ill defined. The cardiothoracic ratio is 0.56 and the mediastinum remains shifted slightly to the right. The diaphragm and intercostal spaces have a normal appearance. A further roentgen study (Fig. 4*D*) was made twenty-seven days after Figure 4*A*. A few minute densities remain in both lungs but the other structures have a normal appearance. The cardiothoracic ratio is 0.52.

This case demonstrates the roentgenographic changes which occur in a newborn infant when an entire lung fails to expand. Twenty-nine days were required for the expansion of the atelectatic lung.

Case v. B. G. R. The patient was a full-term newborn infant who was admitted to Babies and Childrens Hospital at the age of eighteen hours because of cyanosis and rapid, shallow respirations. Birth weight was 3,765 grams. At physical examination the pulse was 200 and respiration 104. The patient was a well nourished infant with shallow, rapid respirations and slight cyanosis. The chest was resonant to percussion and the breath sounds were normal. No rales were heard. The heart sounds were normal and no murmurs were heard.

The therapy consisted of continuous oxygen with three to four minutes of positive pressure every four hours.

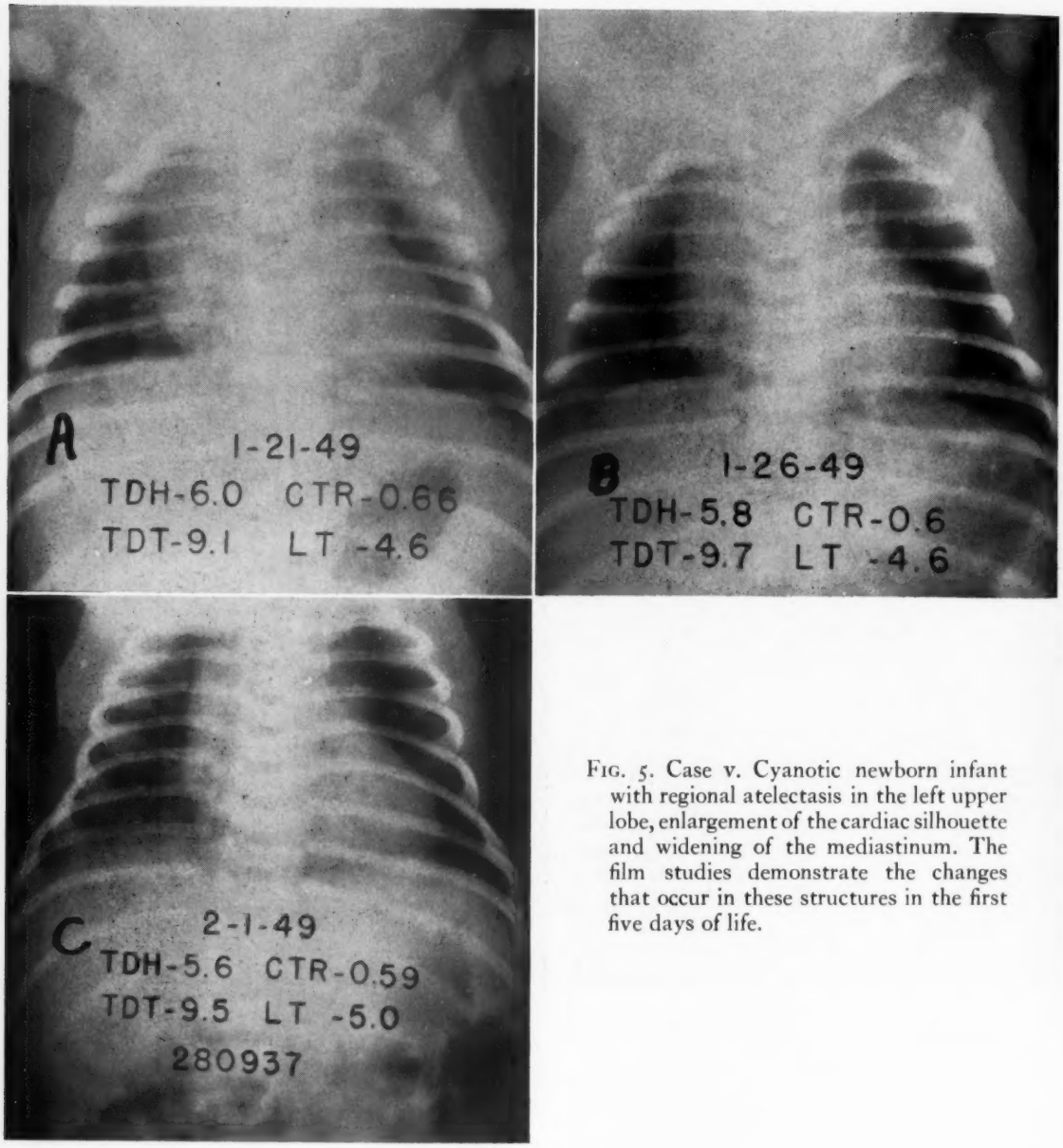


FIG. 5. Case v. Cyanotic newborn infant with regional atelectasis in the left upper lobe, enlargement of the cardiac silhouette and widening of the mediastinum. The film studies demonstrate the changes that occur in these structures in the first five days of life.

*Roentgenographic Findings* (Case 14, Table 11). The chest roentgenogram on the first day of life (Fig. 5*A*) reveals widening of the superior mediastinum. The TDH was 6.0 cm., the CTR was 0.66, the TDT was 9.1 cm., and the LT was 4.6 cm. The lung fields appear clear except for haziness in the apices. A second roentgenogram (Fig. 5*B*) was taken five days after Figure 5*A*. The TDH has decreased to to 5.8 cm., the CTR to 0.60, the TDT has increased to 9.7 cm., and the LT was unchanged. The superior mediastinum has decreased in transverse diameter and the apices of the lungs are better aerated. Figure 5*C* was taken six days after Figure 5*B*. The TDH has decreased to 5.6 cm., the CTR to 0.59, and the TDT to 9.5 cm. The LT has increased to 5.0 cm.

This case demonstrates the decrease in the superior mediastinal shadow and in the transverse diameter of the heart following complete aeration of the lungs.

CASE VI. B. G. F. The patient was a white female infant, aged nine hours, who was admitted to Babies and Childrens Hospital because of difficult respirations and slight

cyanosis. There was some difficulty in resuscitation at the time of delivery. At physical examination the pulse was 120 and respiration 52. Birth weight was 2,925 grams. She was a well nourished newborn infant with a moderately strong cry and slight cyanosis. The chest expansion was equal bilaterally and the percussion note was resonant throughout. There was slight retraction of the lower intercostal spaces. The heart sounds were normal and no murmurs were heard.

The patient was placed in a deep box with continuous oxygen. The patient did well and this therapy was discontinued on the seventh hospital day. The hospital course was uneventful.

*Roentgenographic Findings.* The initial chest roentgenogram (Fig. 6*A*) revealed widespread disseminated atelectasis with fine discrete mottled densities measuring up to two mm. in diameter. The measurements were: TDH—5.0 cm., CTR—0.61, TDT—8.2 cm., and LT—4.8 cm. The patient was re-examined seven days later (Fig. 6*B*) and the TDH was 4.8 cm., the TDT was 9.4 cm., the CTR was 0.51, and the LT was 5.1 cm. The mottled densities in the lungs had cleared by this time.

This case demonstrates the decrease in the transverse diameter of the heart and the cardiothoracic ratio and an increase in the length and transverse diameter of the thorax with the clearing of the disseminated atelectasis. There was no evidence of residual changes in the lungs.

Case vii. B. G. L. The patient was a full term newborn female infant who developed cyanosis and rapid respirations shortly after birth. The birth weight was 2,840 grams. Physical examination showed a moderate degree of cyanosis. There was marked retraction of the chest in inspiration. The breath sounds over the left base were harsh and a few fine crackling rales were heard at the end of inspiration.

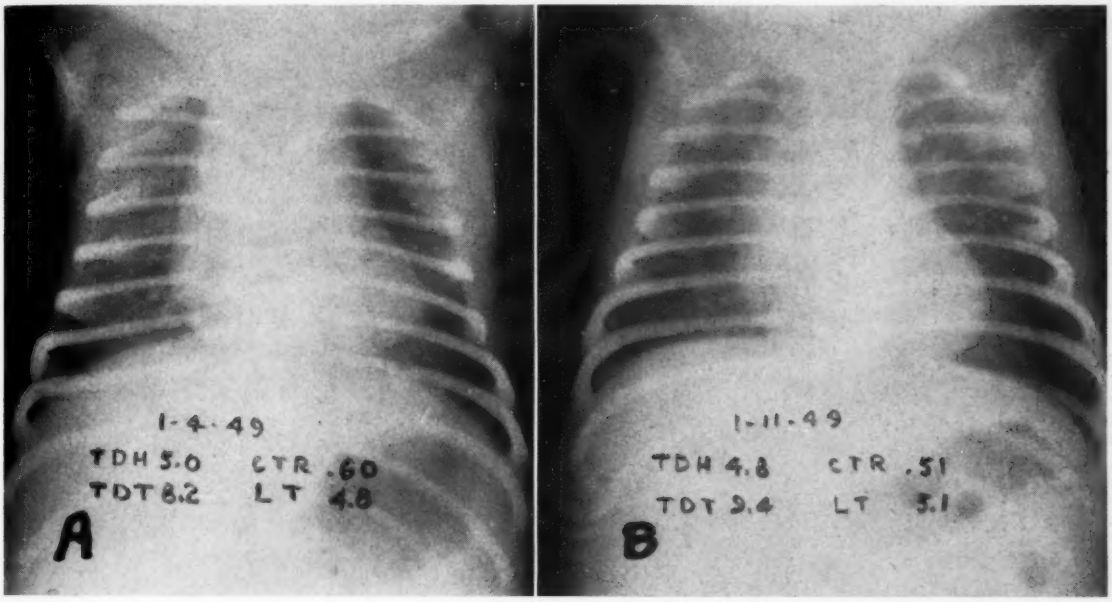


Fig. 6. Case vi. Cyanotic newborn infant with disseminated atelectasis in both lungs, enlargement of the cardiac silhouette and slight flattening of the diaphragm. This case demonstrates the fine, mottled, discrete "salt and pepper" densities in the lungs.

The patient was placed in a deep box with continuous oxygen. The cyanosis gradually diminished, and by the fourth hospital day, the oxygen was discontinued.

*Roentgenographic Findings.* Roentgenograms made on the first day of life (Fig. 7*A* and *B*) reveal coarse, irregular, ill defined densities disseminated throughout both lungs, more marked on the right. Some of the areas are unusually translucent, suggesting the presence of emphysema. The TDH was 5.4 cm., the TDT was 9.0 cm., the CTR was .60, and the LT was 4.8 cm. Roentgenograms taken at the age of four and ten days (Fig. 7*C* and *D*) show that there has been a gradual clearing of the densities in the lungs, a decrease in the

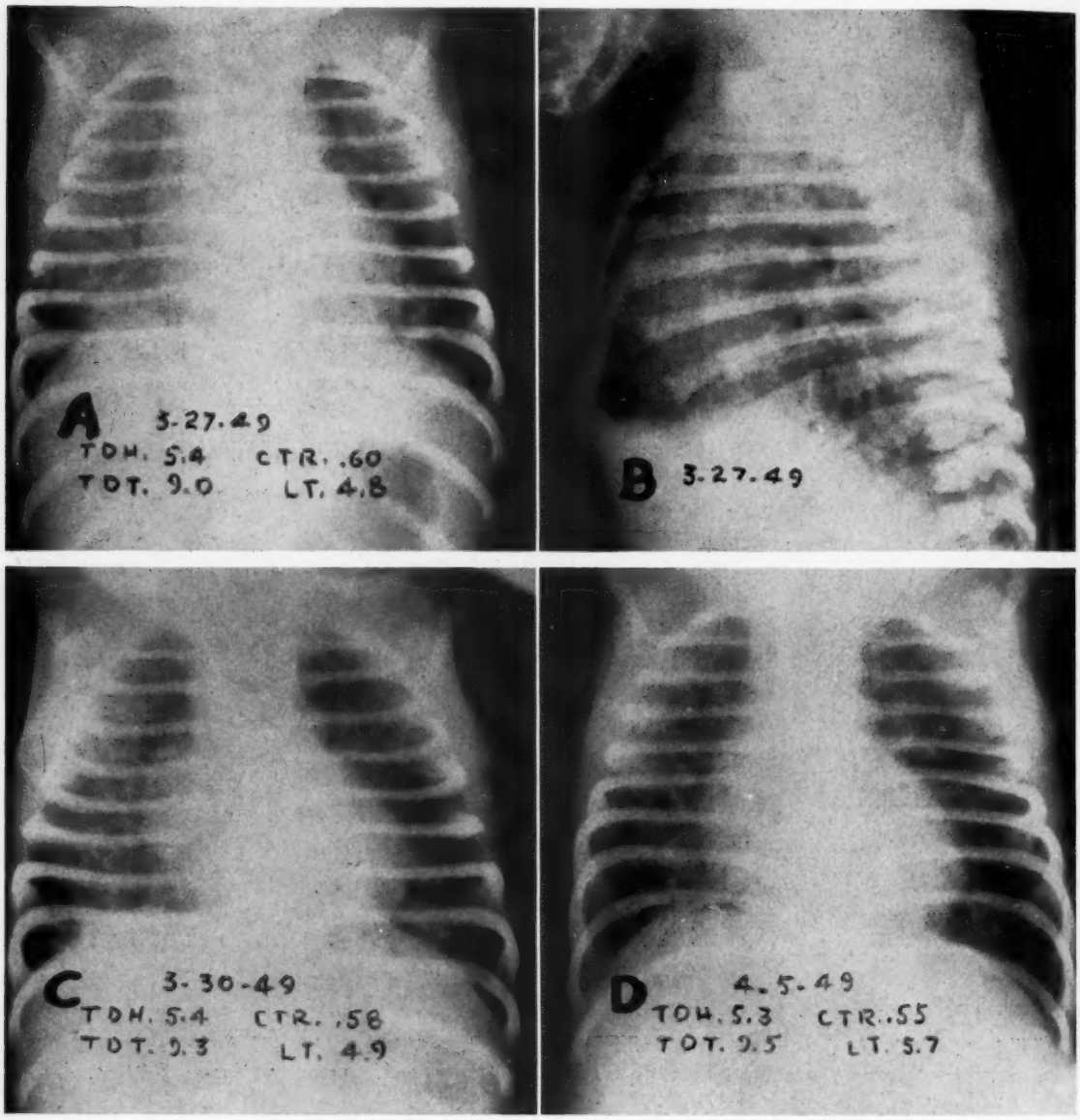


FIG. 7. Case VII. Cyanotic newborn infant with disseminated atelectasis and enlargement of the cardiac silhouette. This case demonstrates the coarse densities seen in the lungs. A film taken after nine days reveals marked clearing of the process.

cardiothoracic ratio, an increase in the length of the thorax and a decrease in the width of the superior mediastinum. On the tenth day, the following measurements were obtained: TDH—5.3 cm., TDT 9.5 cm., CTR .55, and LT—5.7 cm.

CASE VIII. B. G. K. The patient was a newborn infant who was admitted to Babies and Childrens Hospital at the age of twenty-four hours because of periods of cyanosis and abdominal type of breathing.

*Physical Examination.* Temperature, 37.2° C.; pulse, 96; respiration, 56. The infant was in moderate respiratory difficulty with slight cyanosis. The respirations were rapid and shallow. The breath sounds were diminished over the entire right chest and the percussion note was slightly tympanitic. No rales or rhonchi were heard. There was no cardiac murmur. The patient was placed in continuous oxygen with positive pressure for three to four minutes every hour. His color had improved by the second hospital day and the respiratory rate was 35 per

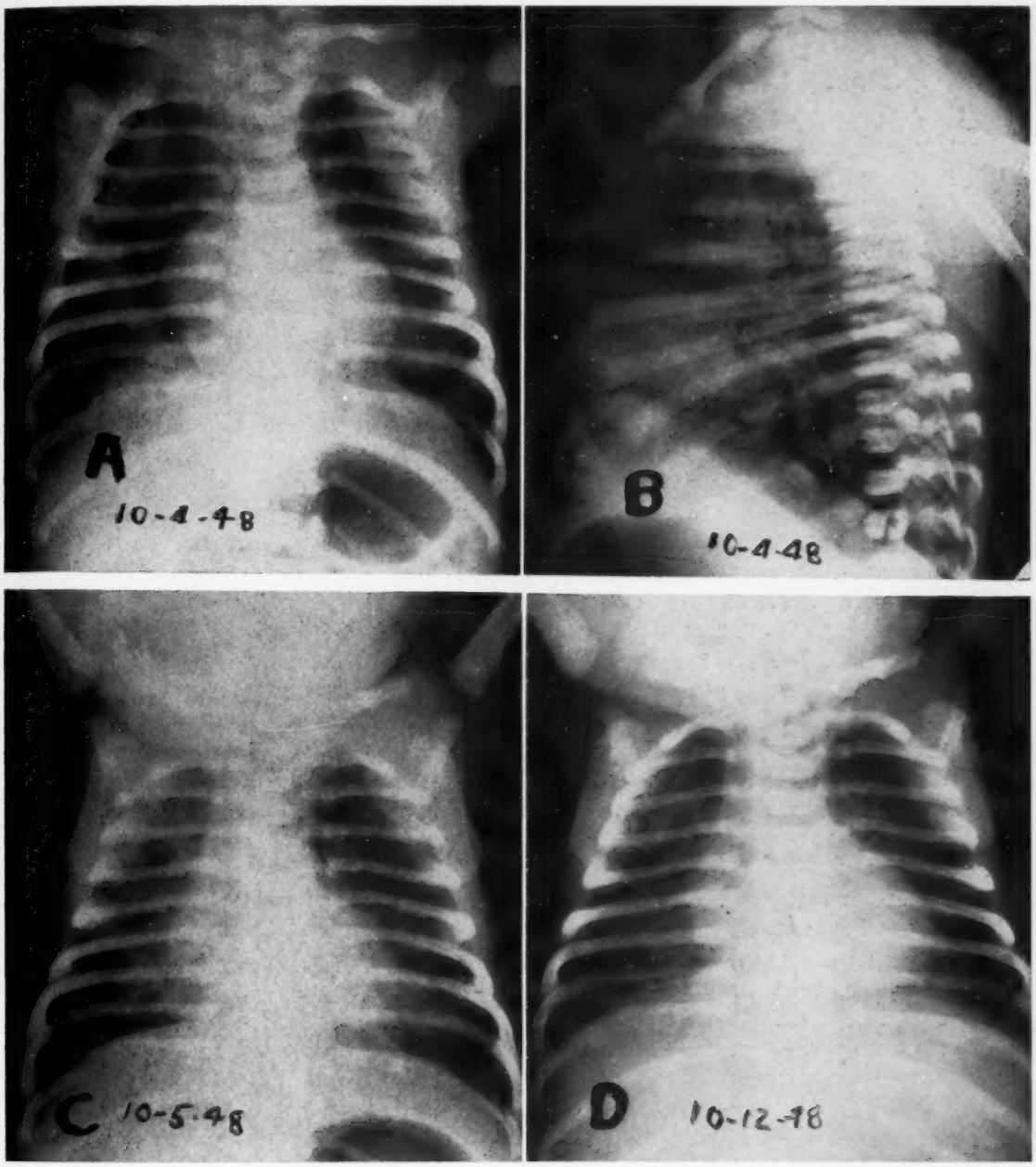


Fig. 8. Case viii. Cyanotic newborn infant with pneumothorax and disseminated atelectasis. The pneumothorax cleared in one day and the lungs were clear in eight days.

minute. The patient was given penicillin (intramuscularly) for eight days. The patient was discharged at the end of ten days with a respiratory rate of 26 per minute.

*Roentgenographic Findings.* The initial study (Fig. 8*A* and *B*) was made on the first day of life and demonstrates partial collapse of the right lung with a moderate amount of air in the right pleural space. The right lung is mottled throughout and the right cardiac margin is sharply defined. Mottled densities are present in the base of the left lung and partially obscure the cardiac margin. The lateral projection demonstrates a moderate amount of air in the anterosuperior mediastinum. Figure 8*C* was made one day after Figure 8*A* and demonstrates complete absorption of the pneumothorax on the right. Numerous

mottled densities persist throughout both lungs and the cardiac margins bilaterally are almost completely obscured. The TDH was 4.9 cm., the TDT was 9.8 cm., the CTR was 0.53, the LT was 5.4 cm. Another roentgenogram (Fig. 8*D*) was made seven days after Figure 8*C*. The lungs by this time had cleared completely and all of the measurements were normal.

This case demonstrates the occurrence of a spontaneous pneumothorax in the newborn infant which is most likely secondary to congenital atelectasis. The pneumothorax was absorbed completely in one day and the atelectasis had cleared at the end of eight days.

## DISCUSSION

The study of the chest roentgenogram in the normal newborn infant reveals that the transverse diameter of the heart and the cardiothoracic ratio decrease in the first three days of life. There was also an increase in the length of the thorax in the first three days of life. There was no significant change in these measurements between the third and fifth days of life. These changes, we believe, are a reflection of the continued initial expansion of the lungs during this period. The lack of a significant change in the measurements on the fifth day of life indicates that the expansion of the lungs was complete at this time.

Scammon[8] has suggested that this decrease in heart size was due to the separation of the placental vascular bed from the vascular bed of the infant. Although this may explain the changes in the normal newborn infant, it does not provide a satisfactory explanation for the increased transverse diameter of the cardiac silhouette in the cyanotic newborn infants.

Bakwin and Bakwin[1] believe that the relatively large transverse diameter of the heart and the large cardiothoracic ratio observed during the first few days of life are due, in large part, to the relative transverse position of the heart. The increase in the length of the thorax in the normal newborn infant during the first three days of life lends some support to this thought. It also indicates that there has been an increase in the volume of the lungs during this period which could only be the result of either increasing expansion of the atelectatic lung or the development of emphysema within the lung. However, since the angle of the heart is related to the position of the diaphragm, and hence to the length of the thorax, it would be expected that this measurement of thoracic length would be significantly different in the cyanotic and normal new born infant groups. A comparison of these measurements in the cyanotic and normal newborn infants on Day 1 (Table IV) reveals no significant difference in the length of the thorax. This leads us to believe that the other factors discussed below must contribute to the increased transverse diameter of the heart and to the increased cardiothoracic ratio. In our studies, and especially in the cyanotic newborn infants, we were unable to measure the angle of the heart with any degree of accuracy from the chest roentgenograms and we are not able to establish the contribution which this makes to the decrease in the transverse diameter of the heart and the cardiothoracic ratio. The cardiac margins, especially those of the base of the heart, were partially obliterated by the thymus gland, while other portions were partially obscured by areas of atelectasis in the lungs.

The findings in the chest roentgeonogram of the cyanotic newborn infant represent an accentuation of the changes observed in the normal newborn infant and are best explained on the basis of incomplete initial expansion of the lungs with its attendant anoxia, tachycardia and altered intrathoracic volume. The cause of the inadequate initial expansion of the lungs is not always clear and a discussion of etiology is beyond the scope of this presentation.

Anoxia accompanies incomplete initial expansion of the lungs because of the lack of sufficient functioning alveoli. The anoxia produces myocardial insufficiency with tachycardia and a progressively decreasing systolic discharge.[6] As a result of such hypodynamic contractions, cardiac dilata-

tion will often occur passively. Evidence of anoxia (subendocardial and subepicardial petechiae) was present in the postmortem studies.

Several compensatory adjustments occurred in the thoracic structures because of the decreased volume of the lungs secondary to initial atelectasis. Although the lungs revealed large homogeneous areas of atelectasis, there was also evidence of emphysema, especially in the basal and peripheral segments. This emphysema is considered to be of a compensatory character. If a segment of a lobe fails to expand, the intrathoracic volume may not be sufficiently altered to cause manifest changes in the remainder of the lungs, bony thorax, mediastinum or diaphragm. This is due to overexpansion of the adjacent aerated lung tissue in an attempt to replace the volume which would have been occupied by the collapsed segment. If an entire lobe fails to expand, the volume deficit is large, approximating one-fourth to one-half of the entire volume of the lung. If the adjacent lung is well aerated, a portion of the volume deficit caused by the unexpanded lobe may be compensated for by overexpansion of the remaining lung tissue, and the abnormal findings in the roentgenogram may be limited to hyperaeration of this part of the lung. A point is reached when the volume deficit of the lung cannot be completely compensated for by overexpansion of the aerated lung tissue and the thoracic structures participate in the compensatory process. This deficit may then be reflected by the well established roentgenographic changes of atelectasis, such as a shift of the mediastinal structures toward the atelectatic lung, narrowing of the intercostal spaces, elevation of the diaphragm on the involved side, and enlargement of the cardiac silhouette.

There is some variation in the roentgenographic findings in congenital atelectasis when compared with those of the resorption type. In congenital atelectasis, a bilateral distribution is much more frequently encountered. The lung findings vary from fine mottled areas of increased density to localized areas of homogeneous density with may be so extensive as to involve an entire lung. These densities may produce either complete or partial obiliteration of the cardiac margins. The mediastinum in the newborn infant is normally wider than later in life and its contour is determined partially by the expansion of the lungs. The mediastinum is shifted when there is a marked degree of atelectasis in one lung.

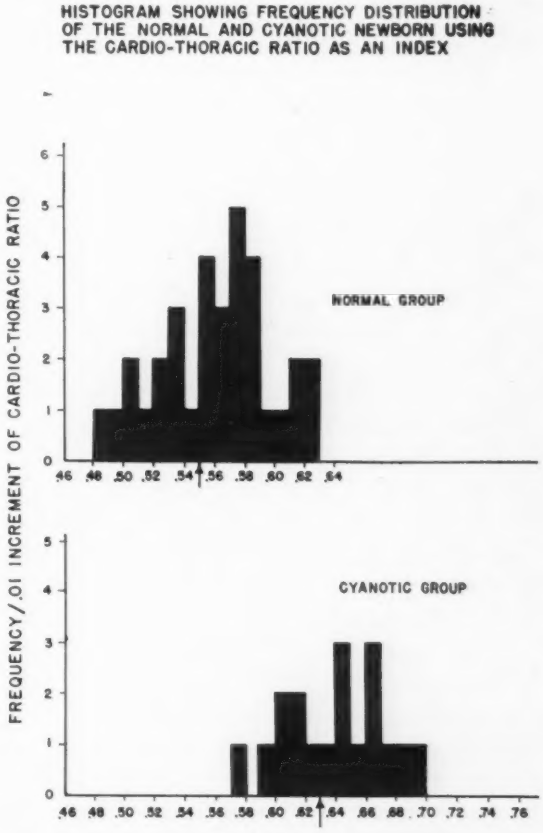
HISTOGRAM SHOWING FREQUENCY DISTRIBUTION OF THE NORMAL AND CYANOTIC NEWBORN USING THE CARDIO-THORACIC RATIO AS AN INDEX
FREQUENCY/.01 INCREMENT OF CARDIO-THORACIC RATIO
NORMAL GROUP
CYANOTIC GROUP
.46 .48 .50 .52 .54 .56 .58 .60 .62 .64
.46 .48 .50 .52 .54 .56 .58 .60 .62 .64 .66 .68 .70 .72 .74 .76

Chart I. Histogram showing frequency distribution of the normal and cyanotic newborn using the cardiothoracic ratio as an index.

There may be no shift of the mediastinum when the distribution is bilateral even though a severe degree of atelectasis is present. Persistent widening of the mediastinum was a more constant feature in these cases of atelectasis than was a shift of the mediastinum. This again emphasizes the findings of Noback[7] in his anatomical study of the thymus gland.

The intercostal spaces may appear normal even though a marked degree of atelectasis is present in both lungs. They become asymmetrical when there is a marked degree of involvement of one lung or when both lungs exhibit different degrees of atelectasis. Generalized deformity of the bony thorax may exist when there is extensive damage to the brain and spinal cord. The diaphragm is usually elevated in the resorption type of atelectasis while in the congenital type it may be elevated, depressed or unchanged. The diaphragm is elevated in congenital atelectasis when there is a severe degree of atelectasis, but occasionally when compensatory emphysema is present it becomes depressed, irregular or flattened. This is especially true if the emphysema is in the basal portions of the lungs.

Enlargement of the cardiac silhouette was a constant feature in the cyanotic newborn infants and is believed to be related to incomplete expansion of the lungs with its attendant anoxia. The intrathoracic pressure decreases abnormally with inspiratory effort when the elasticity of the lungs has been overtaxed by excessive aeration of the expanded alveoli. At such a critical point, the heart and great vessels of the thorax apparently dilate secondary to the decrease in intrathoracic pressure. Wilson and Farber[10] have shown with trachea-lung preparations in the newborn that it may require as much as 35 cm. of water pressure to inflate the bronchi and to overcome the cohesion of the moist surfaces of the bronchi. The differences in pressure required to inflate the non-expanded lung and to dilate the heart and great vessels, or at least to draw more blood into the thorax, probably favors dilatation of the heart and great vessels. The evidence available to us suggests strongly that the degree of cardiac dilatation is related to the degree of non-expansion of the lungs and to the diminished expansile potential of the lungs resulting from compensatory hyperaeration of other portions of the lung. The gradual decrease in cardiac size appears to represent increasing expansion of the atelectatic lung with correction of the emphysema, anoxia and altered intrathoracic volume.

## CONCLUSIONS

1. A study of the roentgenographic findings in congenital atelectasis of the newborn is presented with reference to the changes in the parenchyma of the lungs, the intercostal spaces, the diaphragm, the heart, and mediastinal shadows.

2. Thirty-three full-term newborn infants were studied by chest roentgenograms in the first three days of life. During this period the transverse diameter of the heart and the cardiothoracic ratio diminished significantly. There was no significant change in the measurements when compared on the third and fifth days of life, indicating that the heart of normal full-term infants had reached a state of relative stability by this time.

3. The cardiothoracic ratio and transverse diameter of the heart were significantly larger in the cyanotic full-term newborn infants then in the normal group. These measurements had not returned to normal at the end of four to six days. The increase in heart size is believed to be due to anoxia, tachycardia and altered intrathoracic volume secondary to insufficient initial expansion of the lungs. The cardiac silhouette diminished in size as the atelectatic lung became aerated.

The authors wish to express their appreciation to Corinne S. Cotharin and George S. Badger, M.D., for their aid in the statistical analyses and to the staff members of MacDonald House and Babies and Childrens Hospital for their cooperation in this study.

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# POSITION OF AORTIC ARCH AND DESCENDING AORTA

## ROENTGENOLOGIC SIGNS IN CHILDHOOD*

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THE diagnosis of the position of the aortic arch and descending aorta has become of practical importance since the development of operations designed to create an artificial patent ductus in cyanotic individuals with suitable cardiac anomalies and inadequate pulmonary circulation. In the operation devised by Blalock[5] a subclavian artery is anastomosed to the corresponding branch of the pulmonary artery. Blalock prefers to use the subclavian artery which arises from the innominate artery and is therefore situated on the side opposite to that of the aortic arch. The operation can, however, be performed on either side of the chest and many surgeons prefer to use the left subclavian artery in all cases. An error in diagnosis of the position of the arch in older individuals with subclavian arteries sufficiently large to permit successful anastomosis therefore is not too serious.

In the very young infant, however, the vessels arising from the arch are rarely large enough to permit anastomosis. In such cases it is possible to use the procedure suggested by Potts, Smith and Gibson[8] in which a side-to-side anastomosis is made between the descending aorta and the adjacent main branch of the pulmonary artery. Since it is the hopelessly ill child that would be referred for operation in the early months of life, an error in diagnosis resulting in entrance of the chest by the surgeon on the side opposite to the descending aorta might well prove fatal. An anastomosis could not be performed under such circumstances.

The classic roentgenologic signs by which the presence of right aortic arch can be diagnosed were presented a quarter of a century ago. The first 3 cases reported by Assmann[3] (1924) were all associated with right descending aorta. Assmann described the absence of the aortic knob from its usual position on the left and the presence of an aortic knob situated high on the right side of the sternum. He pointed out the presence of the aortic band above the lumen of the right bronchus as seen in the left anterior oblique position. In the right anterior oblique position, instead of the usual wide aortic band, only a narrow strip of ascending aorta may be seen, the remaining portion of the arch not being visible through the shadow of the trachea. Arkin[1] (1926) published the first description of the roentgenographic appearance of a right aortic arch with left descending aorta. He stressed the use of a barium swallow to visualize the position of the esophagus which is deviated anteriorly and to the left at the level of the arch. He also described the anterior deviation of the trachea, but not until later[2] (1936) did he mention the lateral deviation to the left. Lian and Marchal[6] (1937) stressed a sign which they call "apparent inversion of the bronchi." Normally, when the arch passes over the left bronchus, the trachea is deviated slightly to the right. The axis of the trachea is continued almost vertically into the *right* bronchus, the left bronchus lying almost at a right angle to the trachea. When the arch passes over the right bronchus, the trachea is deviated slightly to the left. The axis of the trachea is continued almost vertically into the *left* bronchus, the right bronchus being almost at right angles to the trachea. This "apparent inversion of the bronchi," according to Lian and Marchal, can be noted in oblique views in which

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the position of the right and left bronchi seems inverted. A summary of the roentgenologic findings to be noted in the various positions of the chest has been presented by McGibbon.[7]

It is not the purpose of the present paper to present new criteria wherewith the position of the aortic arch can be determined, but rather to stress the diagnostic features that have been of value to the author in the study of infants and young children. In infants and children below the age of eight, an aortic knob is rarely seen, so that the absence of a knob on the left is no clue to the presence of a right aortic arch. In a relatively small percentage of children with right aortic arch, a rounded pulsating shadow seen high to the right of the sternum may lead one to suspect that the arch is passing over the right bronchus rather than the left. In the majority of cases, however, a right arch projects as a normal appearing, band-like shadow extending upward toward the right clavicle. I have not always been able to recognize in children the inversion of the bronchi mentioned by Lian and Marchal, either in the anteroposterior or oblique views. Nor can the changes in relation of the aorta to the trachea and bronchi mentioned by Assmann be readily visualized in oblique views in young children.

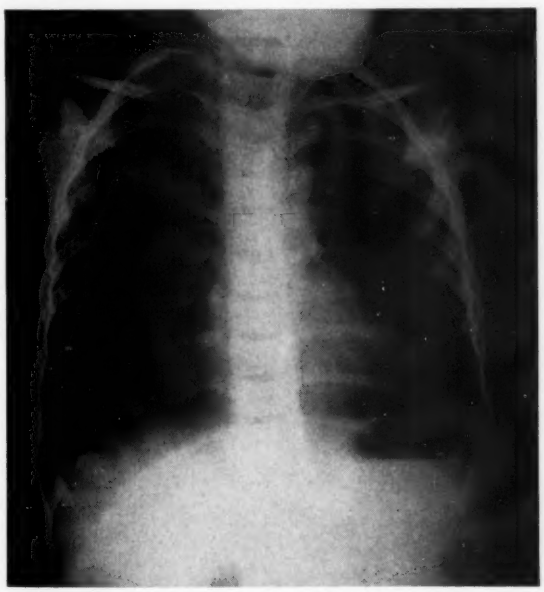

Fig. 1. Left aortic arch with left descending aorta. Deviation of trachea and esophagus to right in the region of the aortic arch. The descending aorta is seen as a narrow shadow to the left of the vertebral column. From a two year old girl with tetralogy of Fallot (proved by operation).

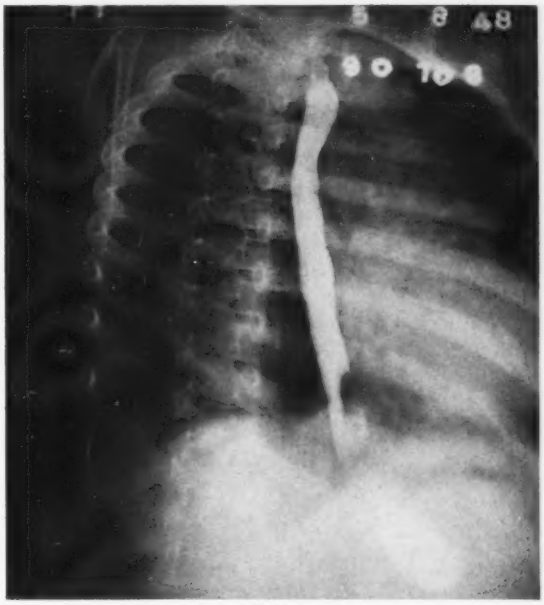

Fig. 2. Left descending aorta associated with left aortic arch. In the right anterior oblique view the esophagus is deviated posteriorly at the level of the aortic arch. From a seven year old boy with tetralogy of Fallot (proved by operation).

The following signs have been of most value in determining the position of the aortic arch and descending aorta in infants and young children:

*Left Aortic Arch with Left Descending Aorta* (Fig. 1).

*Anteroposterior view:* (1) Deviation of the trachea *to the right* in the region of the aortic arch, *i.e.*, just above the division of the trachea into the two main bronchi (best seen in a Bucky diaphragm film, overexposed); (2) deviation of the esophagus *to the right* in the region of the aortic arch (visualized by barium swallow); (3) shadow of the descending aorta along the left side of the vertebral column.

*Right anterior oblique view:* Since the aortic arch passes anteriorly to the esophagus, the latter structure is deviated posteriorly in the region of the aortic arch (Fig. 2).

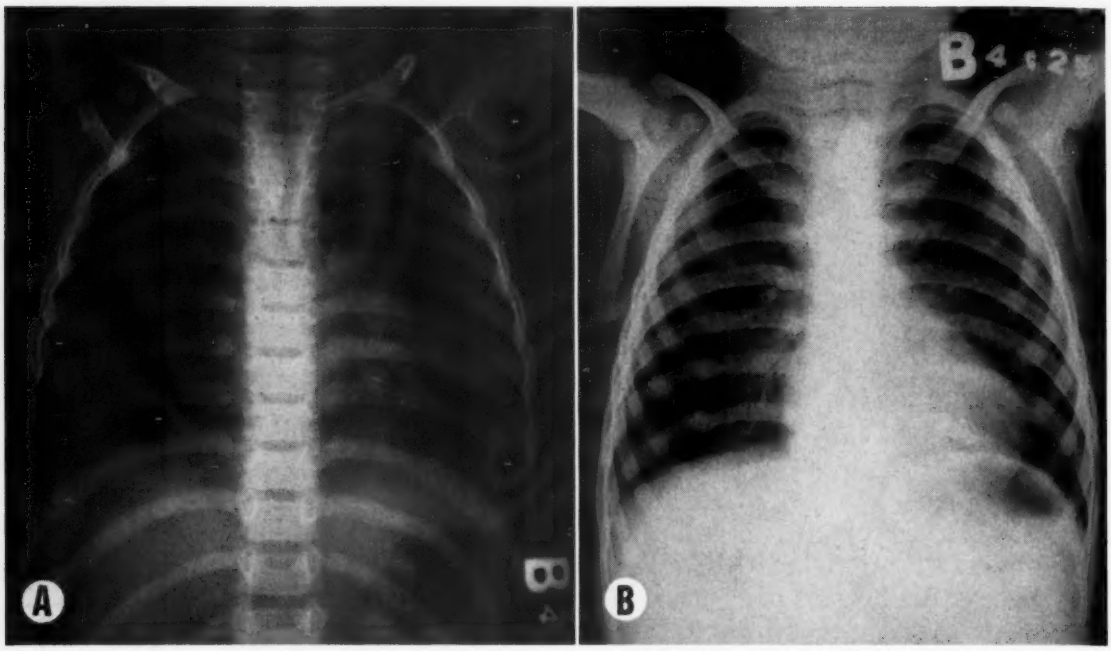


FIG. 3. Right-sided aortic arch. (*A*) Deviation of trachea to left in region of aortic arch. (*B*) Deviation of esophagus to left in region of aortic arch. From a three year old boy with tetralogy of Fallot (proved by operation).

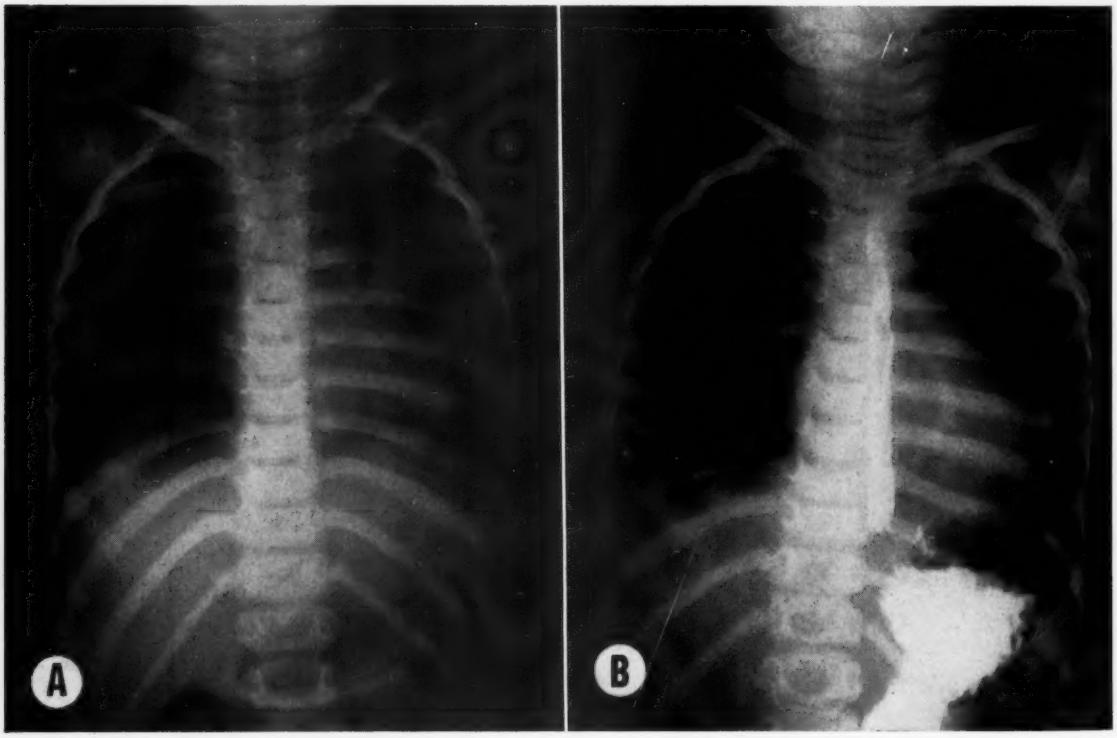


FIG. 4. Right-sided aortic arch. (*A*) Deviation of trachea to left in region of aortic arch. (*B*) Deviation of esophagus to left in region of aortic arch. From a two year old girl with tetralogy of Fallot (proved by operation).

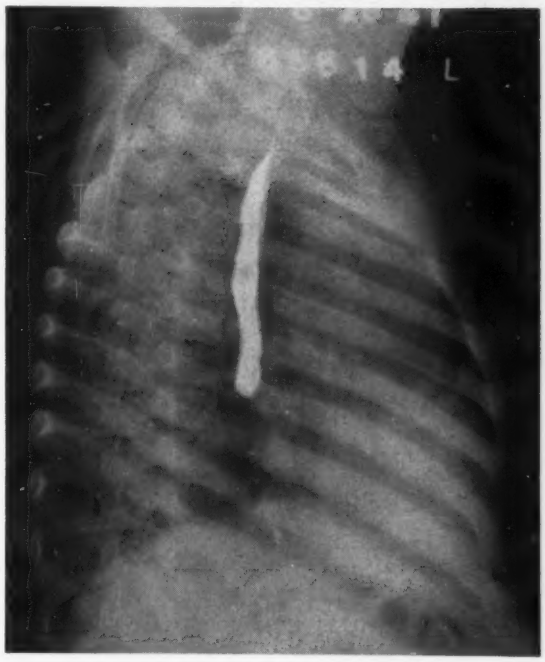

Fig. 5. Right descending aorta associated with right-sided aortic arch. In the right anterior oblique view there is no deviation of the esophagus in the region of the aortic arch. From a two year old girl with tetralogy of Fallot (proved by operation).

*Right Aortic Arch.*

*Anteroposterior view:* Deviation of (1) the trachea and (2) the esophagus *to the left* in the region of the aortic arch (Fig. 3, 4, 6*A*).

(a) With right descending aorta. Absence of shadow of descending aorta along the left side of vertebral column. The aortic shadow may rarely be seen passing along the right side of the vertebral column, but more usually the descending aorta passes in front of the spine and cannot be differentiated.

(b) With left descending aorta. The

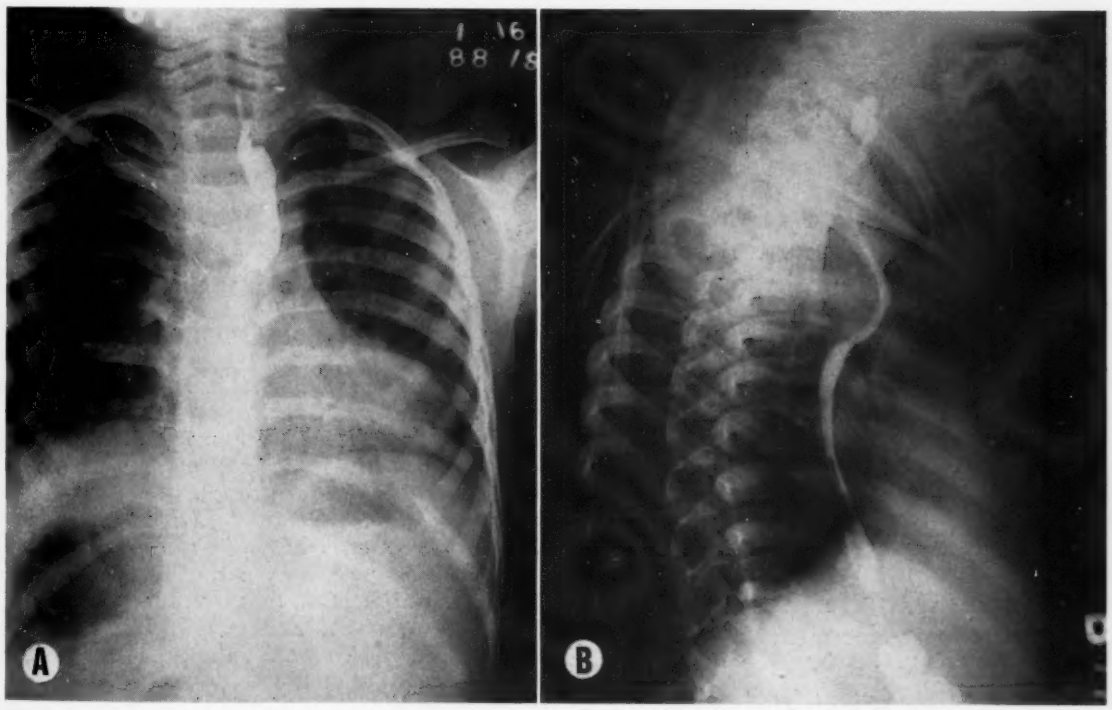


Fig. 6. Right-sided aortic arch with left descending aorta. (*A*) Anteroposterior view: Deviation of esophagus to left in region of aortic arch. The descending aorta is seen as a narrow shadow to the left of the vertebral column. An aortic knob is seen both on the right and the left. (Right-sided arch with left aortic diverticulum.) (*B*) Right anterior oblique view: Deviation of trachea and esophagus anteriorly at level of aortic arch. The shadow of the aorta situated posteriorly to the arch contains a rounded shadow indicating the presence of a left aortic diverticulum. From a five year old boy with no cardiac anomaly (clinical diagnosis).

shadow of the descending aorta may be visible along the left side of the vertebral column (Fig. 6*A*).

*Right anterior oblique view:*

(a) A right descending aorta passes down the chest without contacting the esophagus. There is *no* deviation of the esophagus at the level of the arch (Fig. 5).

(b) If the aorta passes retroesophageally and descends on the left, *anterior* deviation of the esophagus and trachea may be noted at the level of the aortic arch (Fig. 6*B*).

In recent publications major emphasis has been placed on the use of a barium swallow to visualize deviation of the esophagus as an aid in the diagnosis of the position of the aortic arch.[4,9] This is a valuable procedure in older individuals from whom cooperation can be obtained. When one is dealing with seriously ill or uncooperative infants and young children who cannot or will not swallow barium mixture, it is often difficult or impossible to obtain good esophagrams. Many cyanotic infants are too ill even to tolerate the passage of a catheter through which lipiodol can be instilled into the esophagus. It is not too hazardous a procedure, however, in such infants to obtain an overexposed Bucky diaphragm roentgenogram that will present good visualization of the trachea. Although visualization of the esophagus is of value and should be obtained whenever possible it should be emphasized that equivalent information can be obtained by noting the position of the trachea.

In the cyanotic infant in whom it is contemplated to perform a Potts procedure and whose condition seems too precarious to warrant exposure out of oxygen for any length of time, it may be possible to obtain satisfactory visualization of the trachea in an anteroposterior roentgenogram taken with a portable machine. Practically all cases of right aortic arch in association with tetralogy of Fallot are associated with a right descending aorta; similarly, practically all cases of left aortic arch are associated with a left descending aorta. The possibility of retroesophageal crossing of the aorta to the opposite side exists to so slight an extent as to be disregarded for all practical purposes. Deviation of the trachea to the right just above the bifurcation of the bronchi would therefore indicate the presence of a left aortic arch probably associated with a left descending aorta, whereas deviation of the trachea to the left at the level of the arch would indicate the presence of a right aortic arch, probably associated with a right descending aorta.

SUMMARY

The diagnostic features of most value in determining the position of the aortic arch and descending aorta in children have been summarized. In young infants, visualization of the position of the trachea at the level of the arch is stressed as the most helpful guide.

I am indebted to Dr. Ralph S. Bromer for permission to use the roentgenograms presented in this paper.

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Vol. 67, No. 6

# SEPARATION OF THE BLOOD VESSELS FROM THE WALLS OF A LATERAL VENTRICLE IN RAPIDLY PROGRESSING HYDROCEPHALUS*

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PNEUMOENCEPHALOGRAMS of normal or moderately dilated lateral cerebral ventricles usually portray these chambers as smooth cavities. With moderate or advanced hydrocephalus, however, ribbing of the roofs of the lateral ventricles may be observed. Dyke and Davidoff[1] ascribed this scalloped appearance to blood vessels along the apex of each ridge. They postulated that the difference in elasticity or resistance to stretching of the white matter as compared with the same properties of blood vessels resulted in elongation of the vessels up to their limit of elasticity. After this, the ventricular walls continued to recede between the blood vessels except where the resistance of the vessels to further stretching protected the brain tissue adherent to them.

The case reported here supports the concept of Dyke and Davidoff because it demonstrates in vivo that blood vessels were separated from the roof of a lateral ventricle which had dilated rapidly, thereby showing that a difference in elasticity exists between these structures.

## REPORT OF A CASE

M. C., a six week old female infant, was admitted to the hospital because of vomiting and generalized convulsions. The neonatal history had been normal up until the first convulsion five days before admission. The seizures were repeated several times, accompanied by divergence of the eyes, spasticity of the arms, clenching of the fists and an opisthotonic position at the end of the episode.

The child's head was normal in size when first seen, measuring 37 cm. in circumference. The fontanelles were normal. The knee jerks were hyperactive and a sustained ankle clonus was present. Spinal tap produced bloody fluid which was xanthochromic. The protein content was 140 mg. per cent, and the sugar content was over 50 mg. per cent. No further episodes occurred for three days, but spasticity of the lower extremities and bilateral ankle clonus persisted.

On the third hospital day her temperature rose to 101.5° F. and then to 103° F. No positive physical findings to account for the fever were noted. On the sixth hospital day her temperature returned to normal, but she became very irritable and assumed a staring expression. The ankle clonus became less marked but hypertonicity persisted. Eighteen days after admission her head measured 41.3 cm. in circumference, an increase of 4.3 cm.

The clinical diagnosis was subarachnoid bleeding. The neurosurgical consultant (Dr. I. M. Tarlov) believed that the hydrocephalus was due to basal arachnoiditis secondary to

FIG. 1a. Left lateral prone ventriculogram showing dilatation of the right lateral ventricle. Strands (arrows) across the atrium are visible. At the points of merging of the strands and the roof of the ventricle a downward ribbing (A) can be seen. The strands also lead to the tumor mass in the region of the choroid plexus (B).

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FIG. 1b. Postercanterior prone ventriculogram. The strands across the right lateral ventricle are indicated by arrows, and the ribbing of the ventricular walls are marked "A."

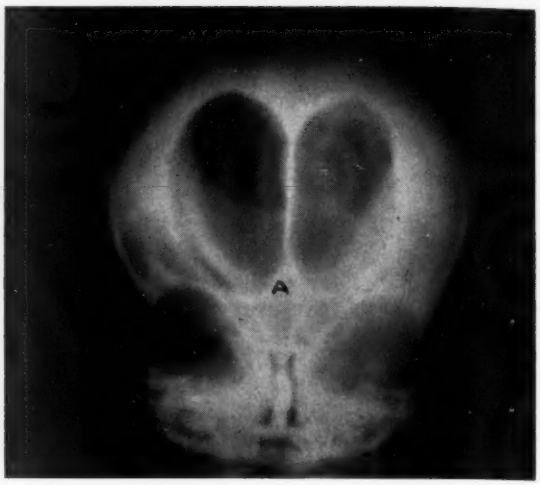

FIG. 1c. Anteroposterior supine ventriculogram. The lateral ventricles are in the midline, and are dilated. The third ventricle (A) is also dilated and in the midline.

hemorrhage resulting possibly from rupture of a congenital aneurysm.

Plain roentgenograms of the skull taken on the day of admission showed no bony changes. The suture lines were normal. Ventriculograms made sixteen days later showed that the skull had increased perceptibly in size. The anterior fontanelle bulged upwards and the suture lines were considerably wider. The length of the skull measured from the bregma to the apex of the lambda was 1.5 cm. longer than on the admission films. Advanced dilatation of the lateral ventricles, including the temporal horns, was present. No displacement from the midline was seen. The third ventricle was visualized in the frontal projections, and measured 2 cm. at its widest part. The third and fourth ventricles could not be seen in the lateral views. The cortex of the brain measured 2.5 cm. in thickness in the frontal region and 1.3 cm. in the posterior parietal region. A soft tissue mass indicative of a tumor was present in the floor of the atrium of the right lateral ventricle. Traversing the posterior part of the body of the right lateral ventricle were several linear shadows, best seen in the lateral films. These appeared as strands across the atrium. At the apparent point of insertion of each strand a downward ribbing of the roof of the ventricle was present. It was believed that these were unusual and atypical blood vessels.

At operation the dura was found to be under considerable tension. The brain cortex was 2.5 cm. thick. The right lateral ventricle was entered through a cortical incision and a massive tumor arising from the ependyma of the ventricle was encountered. The bulk of the tumor lay free in the ventricle, and the choroid plexus was incorporated into the mass. The growth was reddish brown in color and friable. Most of the tumor was removed but some tissue was left at the points of attachment. The roof and lateral wall of the ventricle presented a peculiar configuration comprised of elevation and depressions. Across some of the depressions, a number of blood vessels bridged the gaps. These were bright red, and when the surgeon's head lamp was directed towards the cavity they appeared like a brilliant red network of strings from 2 to 3 mm. in diameter crossing the vaulted roof of the lateral ventricle.

Microscopic examination of the tumor revealed an undifferentiated glioma of a mixed cell type. The majority of cells resembled spongioblasts, and less commonly astrocytes. In a few places there was a cannular arrangement of cells suggesting ependymal formations (Dr. Tarlov).

The child died at another hospital four months later.

## COMMENT

The vascular supply to the lining of the lateral ventricles is from the anterior and posterior choroidal arteries. Observations of several fixed specimens of normal children's brains showed these vessels to be

very small. Similar findings were noted in normal adult brains. It is not possible, however, to gauge with any semblance of accuracy the actual size of these vessels from such postmortem examinations. Nevertheless, the size of the vessels observed at operation in the patient reported here suggests that they were considerably dilated. The fact that these vessels traversed the lateral ventricle entirely free from its roof, extending between the lateral wall of the atrium, the medial wall and the tumor mass indicates that the receding brain tissue must have been torn free. This indicates that under the strain of a rapidly progressive hydrocephalus a definite difference in the resistance of the white matter and the blood vessels to the strain of advancing dilatation exists.

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# CARCINOMA OF THE CARDIA OF THE STOMACH AS DETECTED BY LAMINAGRAPHY*

*By* ROBERT L. FRIEDMAN, M.D.,† *and* MILTON G. WASCH, M.D.
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CARCINOMA of the cardia of the stomach too frequently provides a diagnostic puzzle which is not solved until the disease has progressed beyond the limits of operability. The solution of the problem is to arrive at the diagnosis while the lesion can still be removed surgically. With this in view, an attempt was made to employ laminagraphy with air inflation of the cardia as a means of earlier diagnosis.

In a series of articles evaluating laminagraphy, Moore[3,4,5,6] wrote that this method of examination had little value in the gastrointestinal tract. Ungar, Spiegler and Smithers[11] employ laminagraphy to great advantage in estimating tumor volume in this region for radiation therapeutic purposes. Weinbren,[13] in his manual, states that laminagraphy of the cardia of the stomach will demonstrate the outlines of the tumor better than control films.

When a definite diagnosis can be made on the routine roentgenoscopic and roentgenographic examinations, no problem arises. It is only when unusual findings at the cardia are noted on the routine study that special roentgen examination is necessary. It is in these cases in which air insufflation is employed by us. We have found that laminagraphy in such instances is a definite asset in visualizing the mass and in determining its extent more precisely. Wasch and Epstein[12] and others[2,7,8,9,10] showed that the positive diagnosis of tumors of the cardia depends on the demonstration of the mass contrasted against the air in the cardia. In the method of Wasch and Epstein the air is introduced by a Levin tube employing a sphygmomanometer bulb.

Following the conventional roentgen examination of the air-filled stomach, the patient is placed on the Kieffer laminagraphic table in the supine position and the stomach re-inflated until he feels the desire to eructate. Films are then taken at various levels, usually in the 10–15 cm. range (from the table top). These reveal the soft tissue tumor in sharp contrast to the air filled cardia, it is usually polypoid and presents a scalloped margin which is rather distinctive, whereas an extrinsic mass encroaching upon the air-filled cardia usually presents smooth borders.

A series of 13 cases was studied as outlined in Table 1. Five illustrative cases are herewith recorded.

## REPORT OF CASES

CASE 1. M. R. (Hosp. No. 332044), white male, aged seventy-five, with hematemesis and melena of twenty-four hours' duration. For the past six months, the patient had pain, occasionally burning in nature, in the right upper quadrant radiating to the back, not related to meals, time of day, nor activity. Two days before admission the patient developed nausea, and two hours before entering the hospital he suddenly felt a cold sweat, weakness, and vomited considerable blood with large clots followed by a tarry stool. He lost 11 pounds in four weeks. The physical examination was negative.

Laboratory examinations were normal except for a hemoglobin of 60 per cent and a 3.15 million red blood cell count. Stool examination for blood was 4 plus. Gastric extraction revealed an absence of free hydrochloric acid, a total acidity of 23, 4 plus blood and a positive lactic acid reaction.

A gastrointestinal series revealed a definite filling defect at the uppermost portion of the lesser curvature adjacent to but apparently not involving the esophageal opening. The finding was characteristic of a gastric carcinoma involving the cardia. A second study, including

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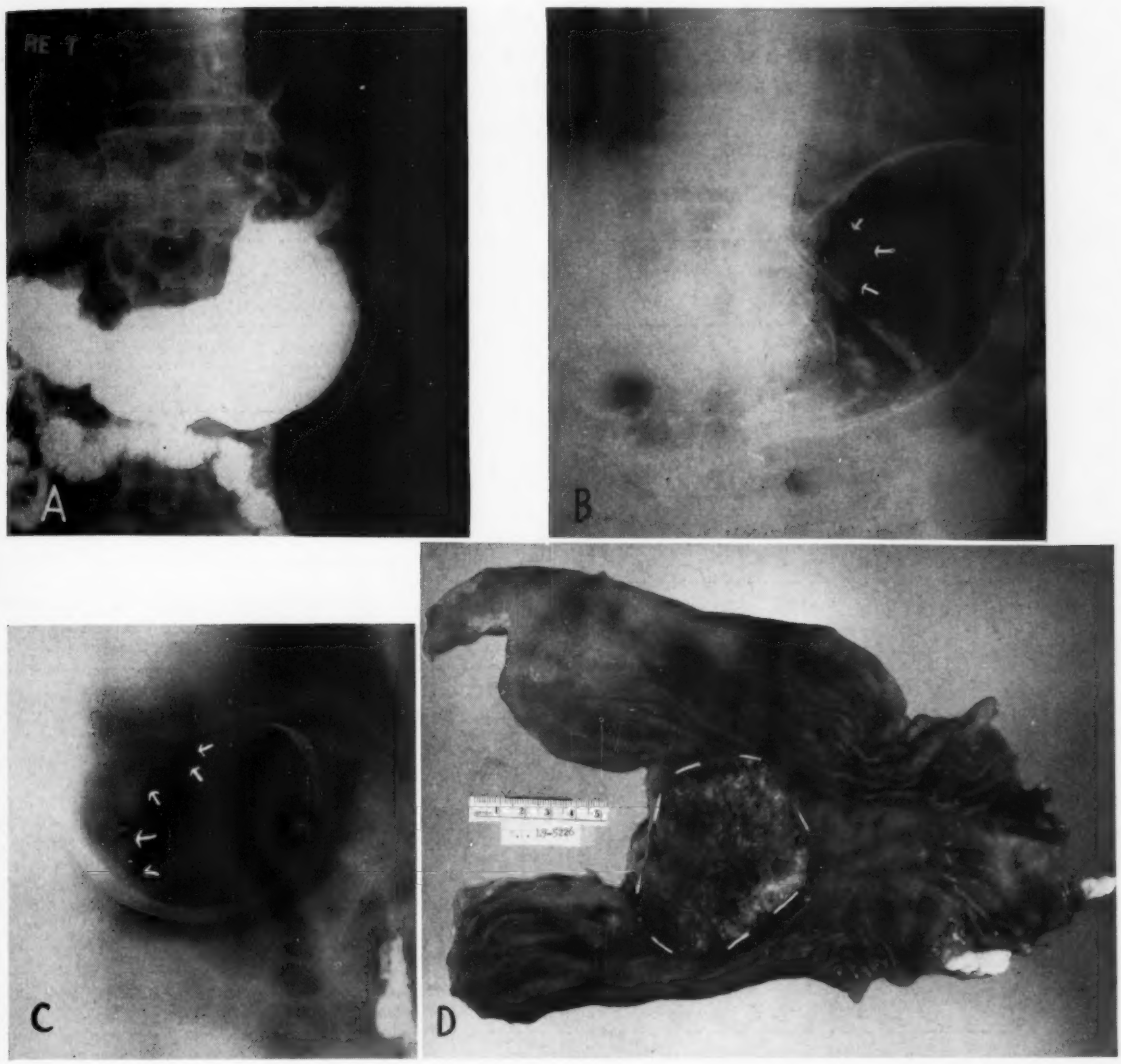


Fig. 1. Case I. (*A*) Erect film showing irregularity of the rugal pattern at the cardia. (*B*) Erect roentgenogram of air-insufflated stomach showing the tumor mass faintly. (*C*) Laminagram of air-distended cardia visualizing clearly the extent of the tumor and its scalloped border. (*D*) Photograph of resected stomach showing cauliflower carcinomatous mass.

air insufflation and laminagraphy, demonstrated a large cauliflower mass best portrayed on the laminagrams (Fig. 1).

Operation revealed a firm ulcerating mass extending from below the cardio-esophageal opening to the mid-portion of the stomach. There were several enlarged inflammatory lymph nodes in the gastrohepatic omentum. A total gastrectomy, splenectomy and an esophagojejunostomy was performed.

The pathological report described the lesion as an oval mass measuring 7 cm. in diameter astride the lesser curvature. Its proximal margin was 0.6 cm. below the amputated end. The mass was firm in some areas, soft in others, and elevated 1 cm. above the mucosa. Diagnosis was adenocarcinoma of the stomach without glandular involvement.

*Comment.* The diagnosis in this case was suggested on the routine roentgen examination but the visualization of the tumor, on laminagraphic study, was distinctive.

Case II. M. T. (Hosp. No. 306631), white male, aged fifty-four, entered the hospital complaining of weakness, exertional dyspnea and numbness of the fingers of three weeks' duration. There was also pain in the calves on walk-

TABLE I

SUMMARY OF THIRTEEN CASES OF CARCINOMA OF CARDIAC END OF STOMACH AS STUDIED BY LAMINAGRAPHY

| Case No. | History | Roentgen Examination |
|---|---|---|
| I. M.R.* Hosp. No. 332044 | Male, aged 75, pain in right upper quadrant, 6 months duration; weight loss, 11 pounds; hematemesis with melena past 24 hours. | Filling defect of uppermost portion of lesser curvature adjacent to, but not involving the esophageal opening. Diagnosis: gastric ulcer of cardia, possibly malignant; laminagrams of air-distended stomach; large, irregular, cauliflower mass within cardia; neoplasm |
| II. M.T.* Hosp. No. 306631 | Male, aged 54, pallor, weakness, and exertional dyspnea for 5 months; dyspnea and numbness of fingers for 3 weeks | Abnormal curvilinear rugal markings at cardiac end of stomach. Diagnosis: negative, gastrointestinal series. Laminagrams of air-distended stomach: large, nodular soft tissue tumor in cardia |
| III. Z.G.* Hosp. No. 312697 | Male, aged 70, weakness, epigastric pain. Fainted, followed by tarry stool 5 weeks before admission; dysphagia for 2 weeks | Gastrointestinal series negative on two occasions. Laminagrams of air-distended stomach negative |
| IV. J.D.* Hosp. No. 310749 | Male, aged 68, burning pain in epigastrium, 38 pound weight loss; vomiting during past 3 weeks with relief of pain | Negative on three occasions except for questionable rigidity of lesser curvature. Laminagrams unsuccessful as air passed into small intestine and stomach was not distended |
| V. F.H.* Hosp. No. 321541 | Female, aged 68, progressive weakness for 6 months. Nausea; vomited a glassful of bright red blood 3 weeks previously | Area of lesser curvature rigid with peristaltic blockage. Laminagrams of air-distended stomach showed smooth, soft tissue tumor mass projecting into fundus above the cardio-esophageal junction |
| VI. B.K. Hosp. No. 331428 | Male, aged 67, generalized abdominal pain, anorexia, and 35 pound weight loss during past 6 months | Irregularity of the lesser curvature and posterior wall, indicative of carcinoma. Laminagrams of air-distended stomach: nodular mass protruding into the cardia |
| VII. M.A. Hosp. No. 321757 | Female, aged 55, 4 months of fever. Weakness, malaise, 16 pound weight loss during past 18 months | Rugal pattern abnormal and the fundus does not distend. Laminagrams of air-distended stomach: nodular margined, orange sized mass visualized protruding into cardia |
| VIII. G.K. Hosp. No. 320112 | Female, aged 59, vomiting after meals for past 4 months. Dysphagia and 10 pound weight loss | Absence of peristalsis and rigidity of upper half of lesser curvature. Laminagrams of air-distended stomach: nodular tumor mass below cardio-esophageal junction |
| IX. I.S. Hosp. No. 311684 | Male, aged 75, vomited bright red blood, tarry stool followed 4 hours before admission. No previous history | Irregular filling defect at cardia. Abnormal 5 hour curvilinear retention in rugal folds at fundus. Laminagrams of air-distended stomach: large sessile tumor on posterolateral wall protruding into cardia |
| X. K.R. Hosp. No. 263562 | Female, aged 76, loss of weight and difficulty on swallowing during the past year | Irregular filling defect of lesser curvature at the cardiac end. Laminagrams of air-distended stomach: small soft tissue tumor mass on the lesser curvature |
| XI. F.W. Hosp. No. 308047 | Female, aged 75, substernal pain, intermittent dysphagia, and 25 pound weight loss. One year history | Irregular rugal pattern of the posterior wall and lesser curvature below esophageal opening. Laminagrams of air-distended stomach: large nodular soft tissue tumor on the lesser curvature protruding into cardia |
| XII. M.S. Hosp. No. 308044 | Male, aged 82, weakness, anorexia, and 10 pound weight loss. Four month history | Large mass at cardia of the stomach. Laminagrams of air-distended stomach: large nodular tumor mass in cardia |
| XIII. J.H. Hosp. No. 311300 | Male, aged 59, epigastric pain for 20 years. Nausea and abdominal distress for 6 months. Vomited red blood 24 hours before admission | Cardiac end of stomach incompletely visualized and deformed. Laminagrams of air-distended stomach: large cauliflower mass in cardia arising from the lesser curvature and posterior wall |

* Case recorded and illustrated in text.

ing, relieved by rest. The hemoglobin was 45 per cent and a diagnosis, following a hematological study, was severe normochromic anemia suggestive of neoplastic disease.

Physical examination was essentially negative except for pallor of the skin and mucous membranes.

Laboratory examinations were negative with the exception of a hemoglobin of 37 per cent and a red blood cell count of 2.33 million. This improved under transfusions to 3.9 million with a rise in the hemoglobin to 78 per cent. Stool was 2 plus for blood on three occasions. Gastric extraction revealed no free hydrochloric acid, a total acidity of 18, 4 plus blood in all specimens, and a positive test for lactic acid.

TABLE I—(*Continued*)

| Operative Findings | Pathology Report |
|---|---|
| Firm ulcerating mass extending from below the cardio-esophageal angle to mid-portion of the stomach; palpable lymph nodes; no liver metastases. Total gastrectomy and splenectomy. Patient died 4 days postoperatively | Oval mass, 7 cm. in diameter, astride the lesser curvature below the esophageal opening. Mass firm in places, soft in others, and elevated 1 cm. above the mucosa. Diagnosis; adenocarcinoma |
| Large firm fungating tumor on the lesser curvature; no metastases; total gastrectomy performed; recurrence 29 months later | Large fungating friable mass on the lesser curvature, 8 by 7.5 by 2 cm., attached to the mucosa by a sessile base. Diagnosis: adenocarcinoma of stomach |
| Firm flat neoplastic mass in the wall of the stomach adjacent to the lesser curvature. Gastrectomy and splenectomy performed. | Flat mass with depressed center adjacent to the lesser curvature, 7 cm. in diameter. Diagnosis: adenocarcinoma of stomach with metastases to the esophagus and lymph nodes |
| Extensive neoplasm of proximal half of the stomach; pancreas and pre-aortic nodes involved; seeding throughout peritoneum; inoperable; biopsy | Diagnosis: portion of omentum with metastatic carcinoma from the stomach |
| No gastric tumor found; hob-nailed liver and enlarged spleen; omentopexy. Discharged 8 days postoperatively | No pathological specimen |
| Firm neoplastic mass in cardia and involving upper half of stomach; spleen and pancreas infiltrated; nodules in liver and diaphragm; inoperable; biopsy | Diagnosis: portion of biopsied omentum with metastic carcinoma from the stomach |
| Refused surgery; treated by roentgen irradiation; mass appeared smaller; fever persisted; discharged; died 6 weeks later; no autopsy | |
| Extensive neoplasm of the stomach involving the pancreas, colon and porta hepatis; biopsy | Diagnosis: lymph nodes with metastatic adenocarcinoma |
| No operation performed | |
| No operation performed | |
| Firm neoplasm, 5 cm. in diameter, on the lesser curvature near cardiac end; direct extension to esophagus, aortic nodes and lesser omentum; inoperable | No specimen removed |
| No operation performed | |
| Proximal to old gastroenterostomy stoma, large neoplasm involving the lesser curvature extending to the cardia; no metastases; gastrectomy and splenectomy performed | Neoplastic mass, 8 by 6 cm., involving the superior edge of gastroenterostomy stoma, and extending proximally along the lesser curvature. Periphery nodular. Diagnosis: adenocarcinoma of stomach |

* Case recorded and illustrated in text.

Roentgen studies of the chest, gallbladder, urinary tract, and colon were negative. The report of the first gastrointestinal series was: "The stomach is normal in size, shape and position. There is a rather unusual curvilinear configuration of the rugal pattern at the cardia but no definite defect can be demonstrated." The series was repeated with air insufflation and subsequent laminagraphy (Fig. 2) which clearly revealed the curvilinear rugal markings as caused by a polypoid lesion visualized as a tumor protruding into the gas-filled cardia.

Laparotomy revealed a large, firm, fungating tumor springing from the upper portion of the lesser curvature, with several firm metastatic

nodes. The liver was not involved. A total gastrectomy was performed.

The pathologist described the lesion as a large, firm, friable mass on the lesser curvature measuring 8 by 7 cm. and extending 2 cm. above the mucosa. The process extended through the serosa involving the gastrohepatic omentum which was adherent thereto. Diagnosis was adenocarcinoma of the stomach with metastatic lymph nodes.

*Comment.* This case demonstrates the value of air insufflation of the stomach in visualizing the tumor mass and again reveals the better detail by means of the laminagraphic study. Roentgenologically the findings might have been considered as atypically normal were it not for this special study.

CASE III. Z. G. (Hosp. No. 312697), white male, aged seventy, in good health previous to present illness. Six weeks before admission the patient fainted upon arising, and a tarry stool followed. There was sharply localized epigastric pain, pressing in nature, not related to food, but relieved by belching and the passing of flatus. The patient lost 10 pounds during this period. Two weeks prior to admission there was intermittent difficulty in swallowing.

Physical examination revealed a loss of subcutaneous fat, and the liver edge was palpable two fingers-breadth below the costal margin.

Esophagoscopy was negative. Gastroscopy was likewise negative, except for a reddened mucosa and an increased amount of mucus.

Laboratory examinations: normal blood findings; the gastric extraction on two occasions two weeks apart revealed free hydrochloric acid 20, total acidity 40, blood varying from 1 to 4 plus in the different samples, and a positive lactic acid reaction.

The gastrointestinal tract, roentgenologically studied on two occasions, including the special studies by air insufflation and laminagraphy, was negative. The esophagus, small intestine and barium enema study of the colon were likewise negative.

Laparotomy revealed a firm flat neoplastic mass in the wall of the stomach adjacent to the lesser curvature about 1 cm. from the esophagus. No secondary deposits were found.

The pathological report described the lesion as a flattened mass along the lesser curvature involving the muscularis and serosa. The lesion was 7 cm. in diameter with depressed center and slightly raised edges projecting 0.5 cm. above the mucosa from which it was sharply demarcated (Fig. 3). Microscopic study revealed an adenocarcinoma with metastases to the lower portion of the esophagus and lymph nodes.

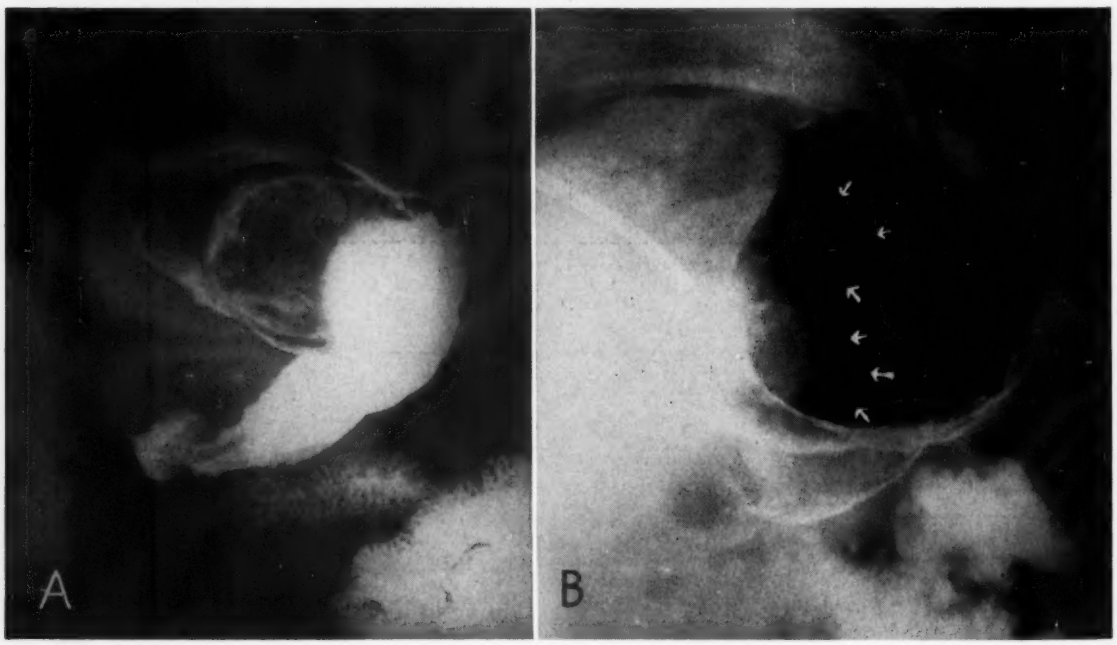


FIG. 2. See legend ⟶

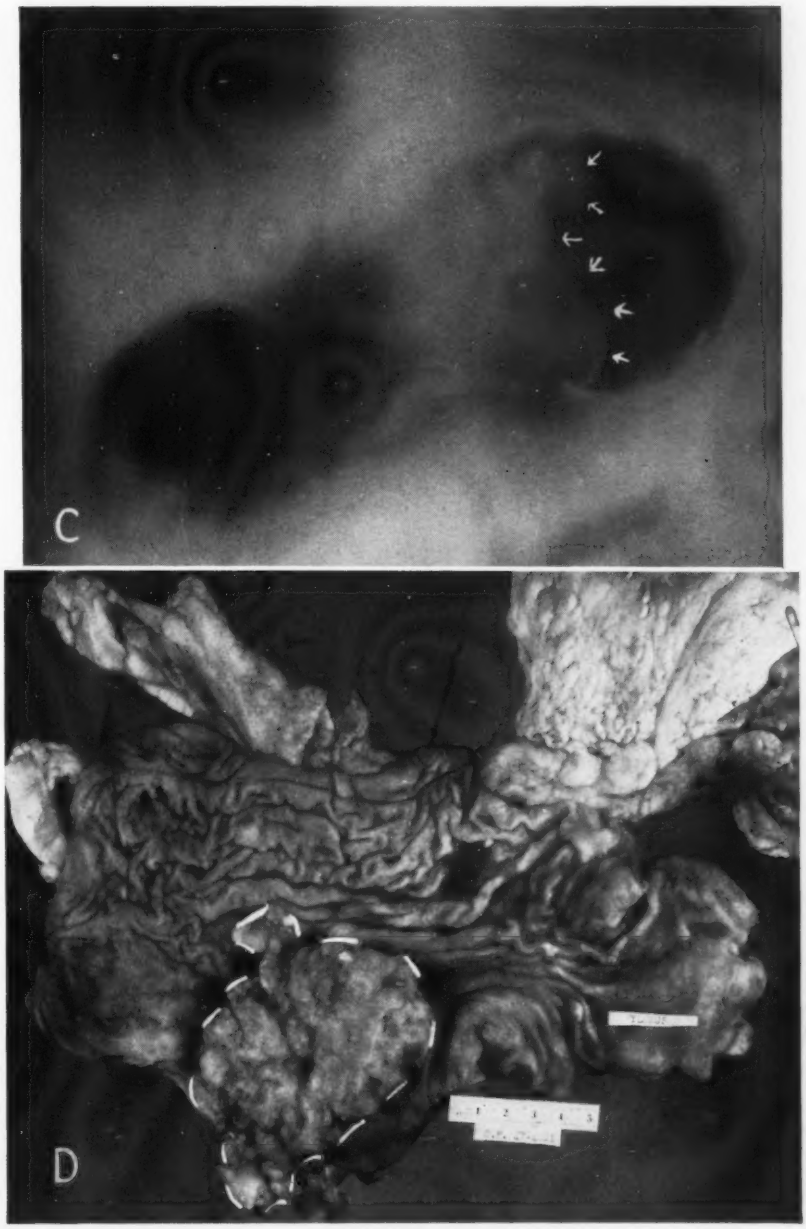


Fig. 2. Case II. (*A*) Right prone oblique roentgenogram showing abnormal curvilinear rugal markings of the cardia. (*B*) Roentgenogram of air-filled cardia portraying tumor. (*C*) Laminagram of air-distended cardia revealing the tumor with its scalloped border more definitely than *B*. (*D*) Photograph of surgical specimen with large nodular tumor outlined.

*Comment.* Despite complete roentgen examination of the stomach, a positive diagnosis was not made. Since the surgical specimen revealed a rather flat neoplasm, with a depressed center, one must be guarded against a non-space-filling defect even though air contrast and laminagraphic films are employed.

Case IV. J. D. (Hosp. No. 279870), white male, aged sixty-eight, complained of a burning pain in the epigastrium of four months' duration. Initially the distress followed meals but later it was concomitant therewith. For the first three weeks, vomiting relieved the pain. He had lost 38 pounds. Physical examination was negative.

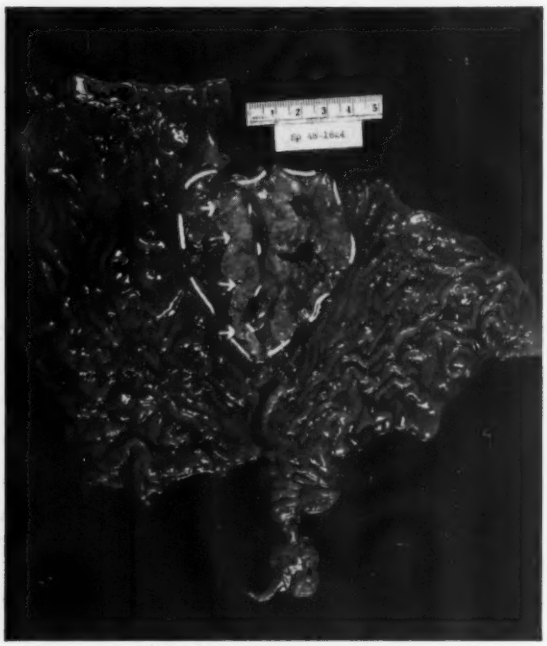

FIG. 3. Case III. Photograph of surgical specimen portraying the plaque-like tumor bisected. Arrows (cut section of tumor) show the thickness of the mass. This tumor was not revealed by air insufflation nor laminagraphy.

Gastroscopy revealed a semi-obstruction at the cardio-esophageal junction, findings consistent with a neoplasm high in the cardia.

Two gastrointestinal series were made as an out-patient and were reported as negative. A third study in the hospital also was negative except for a questionable area of rigidity involving the lesser curvature. The finding was deemed insufficient to be diagnostic. Insufflation was unsuccessful as the air rapidly entered the lesser bowel, the stomach not distending. An infiltrating or gaping pyloric sphincter occasionally accounts for this phenomenon (Fig. 4).

Laparotomy was performed and an extensive neoplasm of the upper half of the stomach was found. The tumor extended posteriorly and involved the pancreas and aortic nodes. There were massive seedings throughout the peritoneal cavity. The case was deemed inoperable and a biopsy was taken. Diagnosis—portion of omentum with metastatic carcinoma.

*Comment.* Roentgen examination in the routine manner failed to visualize the lesion. Special air insufflation studies were attempted but failed due to the patency of the pyloric sphincter and the passage of the air into the small intestine rather than remaining in the stomach and distending it. Work is in progress at this institution employing a balloon to inflate the stomach as an aid in the visualization of cardiac tumors in order to avoid this cause of failure. It is felt that the balloon might also be of value in those cases in which the patient is unable to retain the air.

CASE V. F. H. (Hosp. No. 321541), white female, aged sixty-two, was admitted to the hospital because of progressive weakness of six months' duration. There were intermittent attacks of dizziness and nausea but no vomiting. Three weeks before admission she became nauseated, vomited a glassful of bright red blood, followed by extreme weakness. Recent bone marrow studies were non-informative.

Physical examination revealed generalized abdominal tenderness, most pronounced in the mid-epigastrium. A non-tender liver edge was palpable two fingers-breadth below the costal margin. The spleen extended six fingers-breadth below the costal arch.

Laboratory studies were within normal limits except for a hemoglobin of 50 per cent and a red blood cell count of 2.2 million.

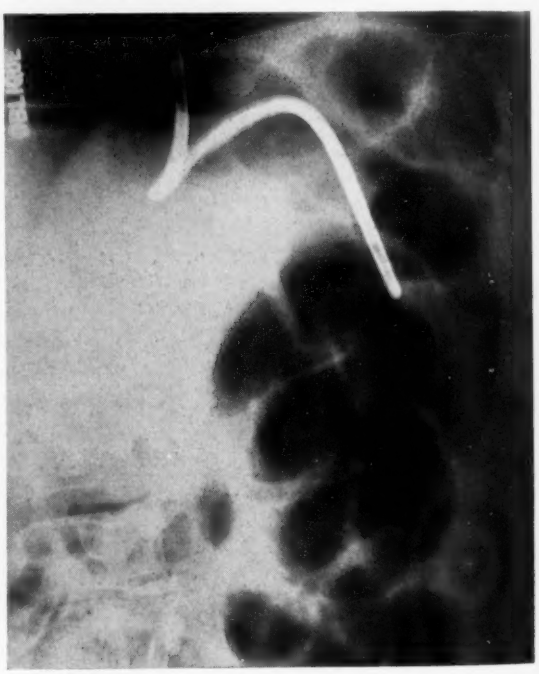

FIG. 4. Case IV. Unsuccessful attempt at air insufflation of the stomach due to loss of pyloric sphinteric action. Air is in lesser bowel loops. Laminagraphy in such instances is of no value.

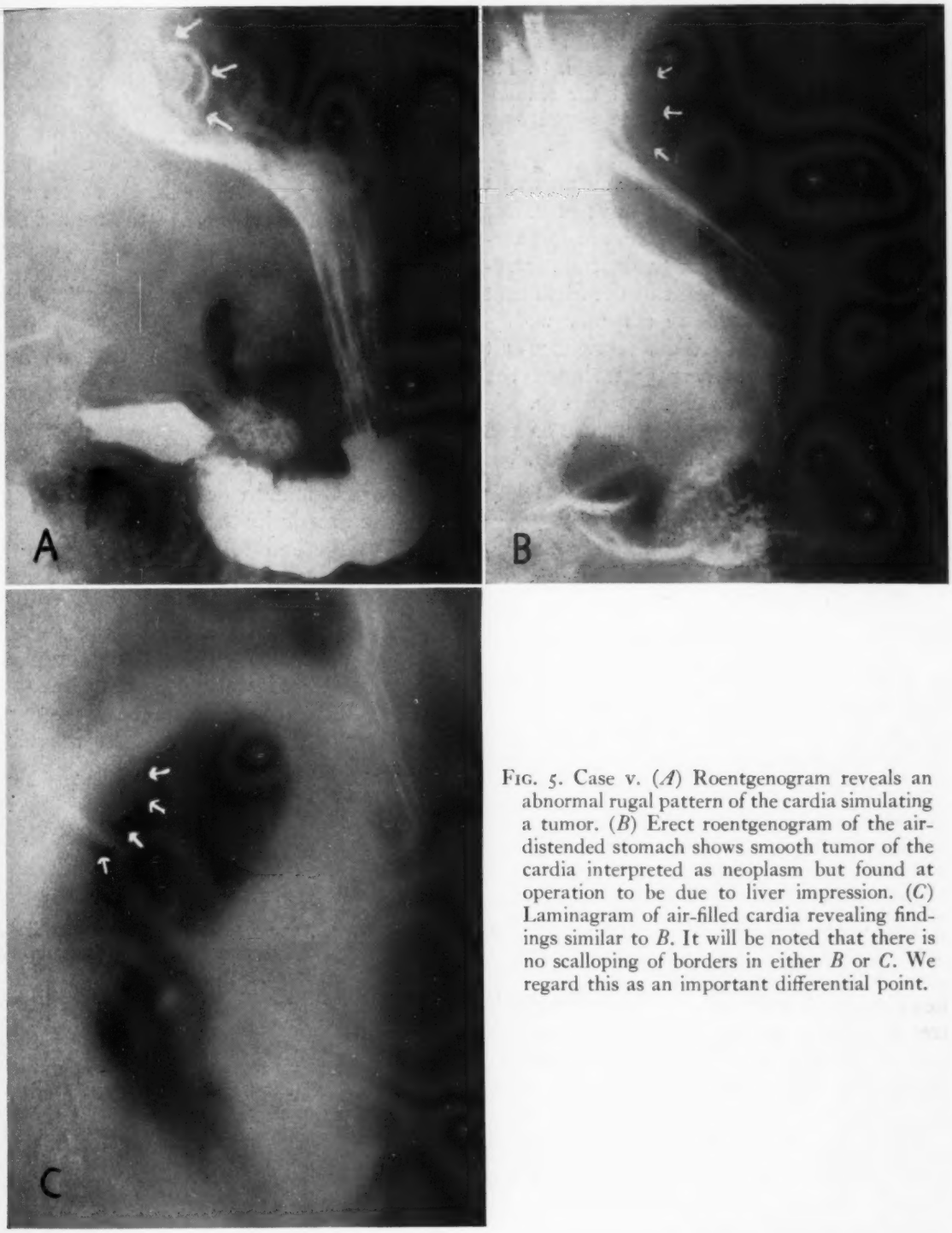


Fig. 5. Case v. (*A*) Roentgenogram reveals an abnormal rugal pattern of the cardia simulating a tumor. (*B*) Erect roentgenogram of the air-distended stomach shows smooth tumor of the cardia interpreted as neoplasm but found at operation to be due to liver impression. (*C*) Laminagram of air-filled cardia revealing findings similar to *B*. It will be noted that there is no scalloping of borders in either *B* or *C*. We regard this as an important differential point.

The gastrointestinal series revealed an area along the lesser curvature where peristaltic waves failed to pass. Due to this area of rigidity a neoplasm was suspected, and a second series with special air studies was performed. This examination revealed a soft tissue mass projecting from the medial portion of the fundus above the cardio-esophageal junction diagnosed as a fundal carcinoma (Fig. 5).

Surgery was advised but refused. She was discharged.

Three months later, because of severe mid-

epigastric pain, the patient was re-admitted for operation. No tumor was found. The liver was enlarged, cirrhotic and hob-nailed. Its imprint upon the cardia produced the shadow seen on the roentgenogram interpreted as a fundal neoplasm.

*Comment.* The failure to reach a correct diagnosis in this case might have been due to the lack of sufficient laminagraphic sections. The presence of a Levin tube introduced an artefact on some of the films that caused the appearance of a tumor with a scalloped border. Additional sections might have avoided this error and shown the smooth contour, thus enabling us to made a diagnosis of extragastric pressure on the fundus rather than intrinsic pathology. We have since experienced a similar type of shadow impinging upon the cardia which proved conclusively by means of air inflation and laminagraphy to be a renal impression.

## CONCLUSIONS

In those cases in which carcinoma of the upper half of the stomach is suspected, in addition to the usual gastrointestinal roentgen series, an attempt should be made to visualize the cardia by means of air insufflation and laminagraphic studies. No roentgen examination of a suspected lesion should be considered complete without them. Hence, we believe that in carcinoma of the cardia of the stomach, as far as earlier diagnosis is concerned, laminagraphy is of great value. We agree with those who believe that this method more clearly visualizes the presence, extent and the configuration of the tumor than the routine roentgenograms made after gastric insufflation alone.

Great care must be given to differential diagnosis, having in mind essentially extragastric tumefaction in the left hypochondrium encroaching upon the stomach wall. We consider the presence of a soft tissue tumor with smooth borders as doubtful of an intrinsic lesion, and feel more convinced of our diagnosis of a gastric neoplasm when a scalloped edge has been demonstrated.

## SUMMARY

1. Thirteen cases of carcinoma of the stomach are reviewed, with an evaluation of air insufflation of the stomach with routine and laminagraphic studies as a means of earlier diagnosis of carcinoma of the cardiac end of the stomach. Of these, ten revealed definite evidence of the tumor, six of which were confirmed by laparotomy; the symptomatology and course of the remaining four cases were clinically beyond doubt. There were three failures by this method: one proved to be cirrhosis of the liver; in the second instance, a patent pylorus prevented a satisfactory outline of the cardia; the third and most disconcerting error was due to a flat serpiginous neoplasm which failed to encroach sufficiently upon the gastric lumen.

2. The method of visualization of the tumor by means of laminagraphy is described.

3. The scalloped margin of the tumor mass, as visualized on the laminagraphic study, is stressed as of diagnostic importance in differentiating an intrinsic tumor mass from extrinsic pressure on the air-filled cardia of the stomach.

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# OIL CONTRAST STUDY OF THE LOWER ESOPHAGUS

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THE roentgen examination of the lower esophagus especially for the detection of varices has in the past not been entirely satisfactory. In spite of continuous technical improvements, small lesions and varicosities in this area can be demonstrated only in a small percentage of cases. Hare[3] was able to show varices in only about 15 per cent of cases which later proved positive at autopsy. Templeton[4] reports demonstrating esophageal varices in 40 per cent of his cases. Figures varying from 15 to 50 per cent have been reported by other investigators.[1]

In order to increase the percentage of correct roentgenological diagnosis of varices and other small lesions, it occurred to me that Gianturco's oil contrast study of the stomach could also be used, in a modified form, for the examination of the lower esophagus. Gianturco[2] recommends that 1/2 glass of barium be followed by an equal amount of mineral oil. This method provides a satisfactory visualization of the gastric mucosal pattern, particularly of the fundus region.

For the oil contrast study of the lower esophagus we have adopted the following technique as a routine procedure:

As part of the usual gastrointestinal series and following roentgenoscopy, the patient is given 2 heaping teaspoons of barium paste of medium thickness and immediately thereafter 2 ounces of extra heavy mineral oil. The usual prone and upright oblique and posteroanterior positions are taken except that views of the lower esophagus must be included on these films.

This provides in all cases for a routine visualization of the lower esophagus and fundus by the double contrast method and serves as a screening for any lesion in this area.

Where special studies of the esophagus are indicated or where esophageal varices are suspected, polygraph views of the lower esophagus are taken as follows:

The barium and mineral oil is given as above. The patient is then placed on the roentgenographic table in an oblique prone position with the xyphoid process in center of a polygraph. Films are taken (1) at rest; (2) in full inspiration; (3) during the Valsalva test; (4) in full expiration (Fig. 1).

If it is desirable to take polygraph views while the patient is swallowing the mineral oil or immediately thereafter, the patient is first positioned on the tunnel and then given the barium and mineral oil as above.

The advantage of this oil contrast method over the ordinary technique is that the mineral oil washes down the excess barium and allows a residual layer to adhere to the wall of the esophagus for as long as five minutes in most cases. Also, the adherent barium and mineral oil coating provide an ideal double contrast for demonstration of the mucosal pattern. The first exposure made immediately after swallowing the mineral oil reveals the esophagus in the dilated stage and with effacement of the mucosal folds. At this stage, one can see the degree of distensibility and elasticity and whether or not there is rigidity in the lower esophagus (see Case 11). These findings are especially valuable when an early infiltrating lesion is suspected. The excess barium and mineral oil at the mixing stage, however, produces occasionally a lumpy granular or vacuolated contrast which is not entirely desirable or helpful for mucosal study. As soon as this excess has emptied into the stomach, the residual barium and mineral oil adhere to the wall so that a sharper and clearer image can be obtained for a longer period than without the mineral oil.

Multiple views at various stages of con-

* Dr. Ernest Kraft, Chief of X-Ray Department.

Fig. 1. Normal "oil contrast" polygraph. (1) At rest; (2) in deep inspiration; (3) Valsalva test; (4) in deep expiration.

traction and relaxation of the esophagus are essential for the demonstration of varices. Unless the veins are visualized while congested, varicosities are missed. This probably accounts for the failure of the roentgenographic diagnosis of varices in cases where they are seen endoscopically or found at postmortem, particularly in early or minimal changes.

So far we have had encouraging results as seen by the following 2 case reports:

## REPORT OF CASES

Case 1. *Esophageal varices.* M. S., white male, aged thirty-six, admitted to Lincoln Hospital on September 15, 1950, because of the sudden vomiting of large amounts of blood without pain, and giving a history of severe similar episodes in the past eight years. During this time he had had intermittent attacks of epigastric burning relieved by alkali. He used to be a heavy drinker. Gastrointestinal series have been persistently negative for peptic

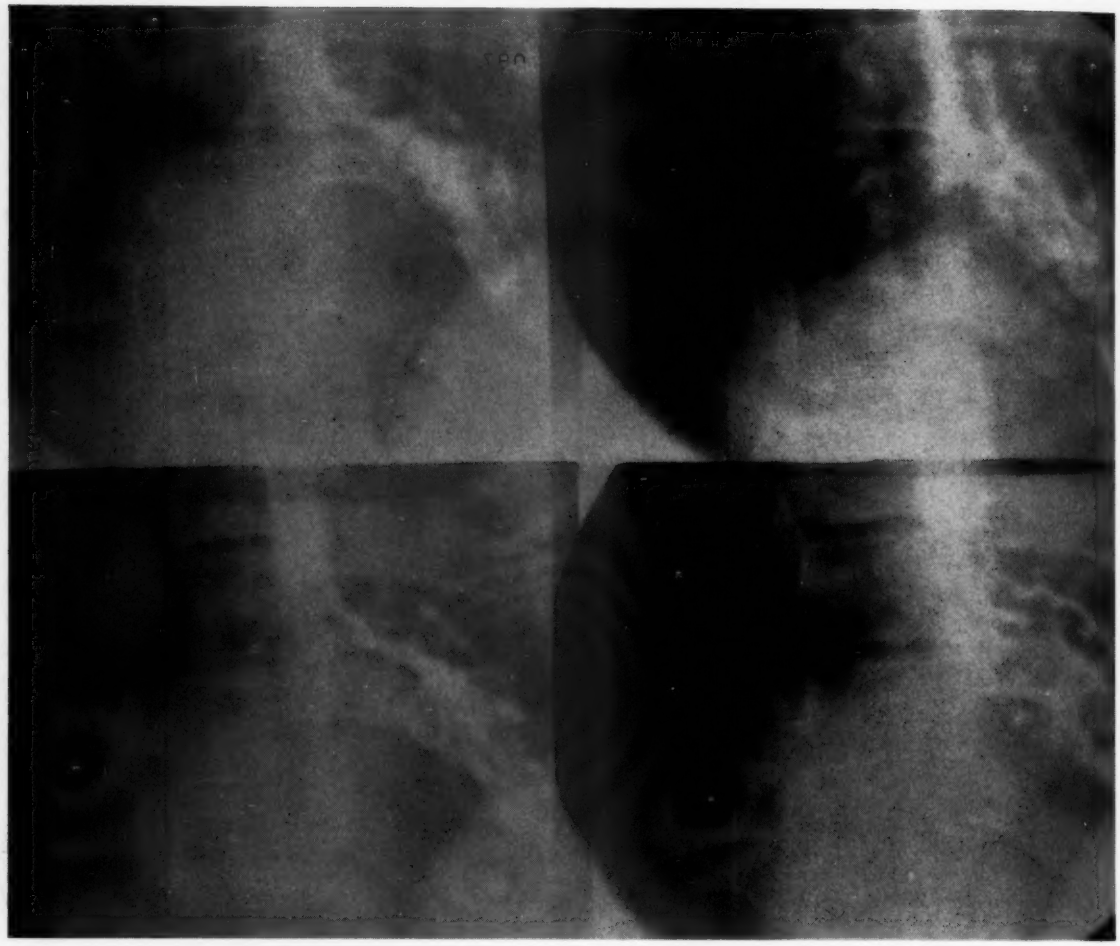

Fig. 2. Case I. Oil contrast polygraph illustrating the presence of esophageal varices.

ulcer. At one time esophageal varices were suspected but never demonstrated. On admission, physical examination was essentially negative except for the acute anemia and an enlarged spleen. The prothrombin time was elevated to twenty-three seconds. The patient was treated with transfusions and vitamin K injections. He improved. A gastrointestinal series and usual esophagus studies done three days after admission showed moderate thickening of the rugae of the esophagus and stomach. Oil contrast study, however, beautifully demonstrated the presence of esophageal varices (Fig. 2).

Case II. *Carcinoma of the esophagus.* C. J., white male, aged sixty-nine, admitted to Lincoln Hospital on January 17, 1951, complaining of vomiting and upper abdominal pains of two weeks' duration. A known alcoholic. Physical examination was essentially negative. Blood chemistry studies favored a diagnosis of cirrhosis of the liver. Roentgenograms were suggestive of a filling defect in the lower esophagus. Esophagoscopy showed mucosal changes reported as varices. Oil contrast films demonstrated the presence of a rigid irregular lower esophagus characteristic of an infiltrating carcinoma. The patient died nine days later of congestive failure. Postmortem examination showed the presence of an infiltrating carcinoma of the lower esophagus, hob nail cirrhosis of the liver and arteriosclerotic heart disease (Fig. 3).

It is hoped that by this method more accurate and earlier diagnosis of esophageal varices may be made; that the diagnosis of hiatus hernia will be simplified, particularly in the small unsuspected cases, and that the early diagnosis of small infiltrating

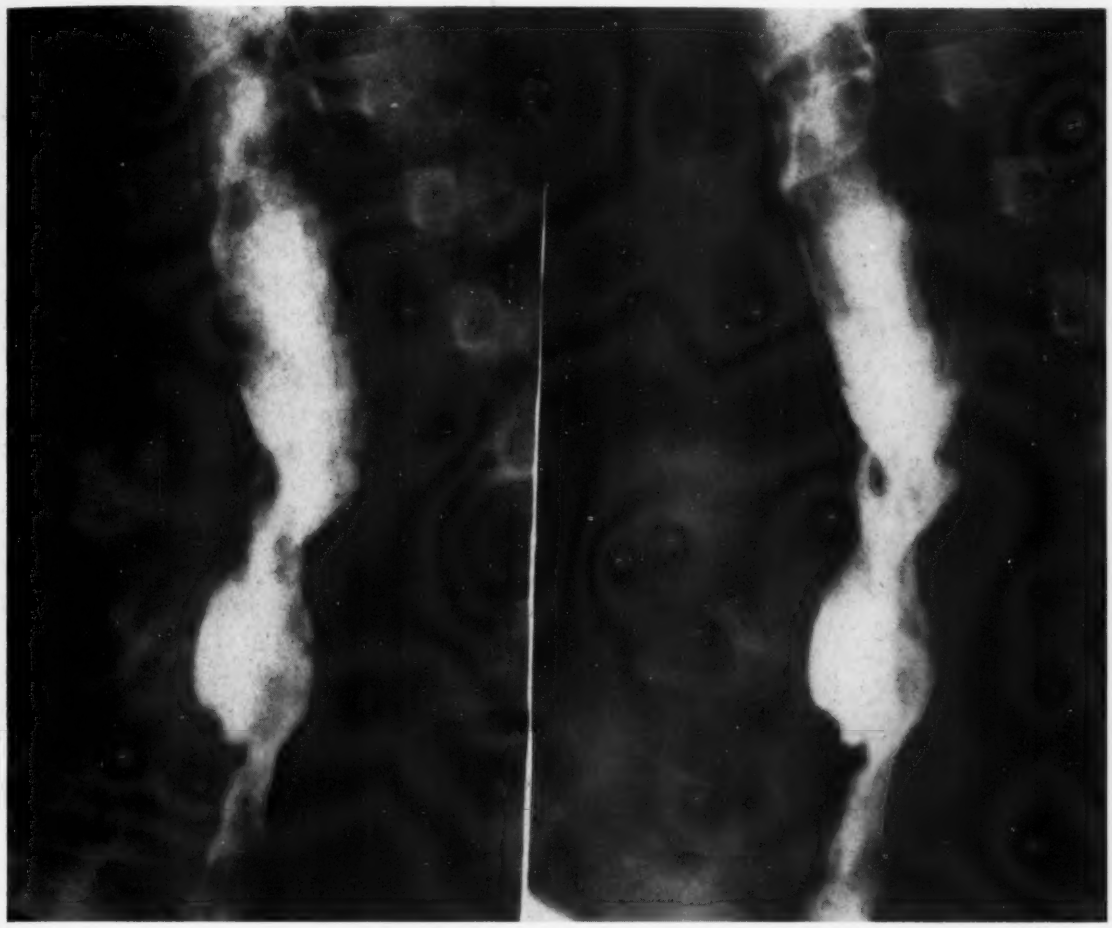

Fig. 3. Case II. Oil contrast views illustrating area of rigidity in the lower esophagus characteristic of an infiltrating carcinoma.

lesions in the lower esophagus may become possible.

Since we have been using this technique routinely, 3 minimal or early cases of esophageal varices have been detected in patients with cirrhosis of the liver where ordinary barium studies had previously failed to disclose pathological changes. Asymptomatic and small hiatus herniae have also been detected by this method which might otherwise have passed unnoticed.

## CONCLUSION

1. A method for oil contrast study of the lower esophagus is described.

2. The method has proved valuable in the detection of esophageal varices, hiatus hernia, and carcinoma of the lower esophagus.

3. Two illustrative cases are reported.

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# THE USE OF FILTERS TO CONTROL RADIATION EXPOSURE TO THE PATIENT IN DIAGNOSTIC ROENTGENOLOGY*

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## INTRODUCTION

THE subject of small doses of radiation exposure to roentgenologists and technicians has received serious consideration over a period of many years. The exposure to the patient, until recently, was considered almost entirely from the standpoint of acute effects, *viz.*, epilation and erythema. So well has this part of the problem been studied and reported that acute effects, as encountered today, are the result of either carelessness or lack of knowledge on the part of untrained workers.

Of more recent interest and concern is the matter of exposure to the patient received during the course of a diagnostic examination. The exposure due to roentgenoscopic examinations has been the subject of many reports, but the exposure received by the patient as a result of the roentgenographic procedure has been studied chiefly from the viewpoint of finding out what intensities and total doses were involved in these procedures. There are a few references in the literature reporting on efforts to reduce the exposure. These have to do chiefly with the influence of distance on the surface dose. While the distance factor has been used effectively in reducing the exposure in roentgenoscopy, it is limited in its application in roentgenography due to the limitation of the Bucky grid which operates effectively over large fields at the distance for which it is designed and none other.

During a period of intense study in the use of high kilovoltage roentgenography a few years ago, it became apparent that the filtration of the beam between the tube and the patient had a marked effect upon the patient exposure. It was also noted that considerable variation in the filtration had little or no effect on the resulting roentgenogram or the factors used to attain it. As a result of these observations, work has been done to study the influence of filtration on the incident beam, the transmission through the part, the dose within the part and the effect on the roentgenogram.

Because of the increased portion of the total population now receiving radiation from so many sources, it may well be that the long term effects of doses too small to produce an acute effect are important. Certain it is that in view of the increased use of radiation in all its forms to such a large percentage of our people, there is an obligation on the part of all who use radiation to subject the patient to as small a dose as is consistent with an adequate examination. Anything that can be done to reduce the dose will be a step in the right direction. The acute effects and well established principles to prevent them were the result of sad experiences to early patients and radiation workers. It is hoped that we will become aware of and establish limitations to prevent the non-acute and long-term effects of small doses of radiation which presently appear to be non-reversible once the effect has been initiated and which may not be restricted in their influence to a single generation.

It is the aim of this paper, along with those who have reported previous work, to make roentgenologists and technicians aware of the influence of some of the roentgenographic factors on this matter of the diagnostic patient dose.

## EQUIPMENT AND INSTRUMENTS

The equipment used for this study con-

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sisted of a 130 kv. (peak), 500 ma., full wave, 60 cycle diagnostic unit of conventional design, a high voltage rotating anode tube and a fixed focus tube. The roentgen-ray table was equipped with a 16:1 reciprocating grid and a phototimer. The phototimer was used for exposures up to 100 kv. (peak). Above 100 kv. (peak) an impulse timer was used. A Standard Electric Time Company Cycle Counter was connected to the phototimer to determine the exposure time as controlled by the phototimer.

All physical measurements were made using a 25 r Victoreen thimble chamber which had been calibrated at the National Bureau of Standards at voltages from 10 kv. to 1 mev. at half-value layers of 0.06 millimeter of aluminum to 4 millimeters of lead. The 25 r chamber was used with a charging and reading instrument having a null-type amplifier making it possible to read changes in chamber potential of as little as 1 volt full scale.

For phantom studies a phantom made of a loaded plastic material devised by D. E. A. Jones was used.

### INTENSITY OF BEAMS

The influence of the inherent filtration of the roentgen tube and of added filter on the intensity of the incident beam was the first subject studied. Our results did not vary greatly from that reported by other workers, most of whom had reported the intensity in connection with studies of the dose received in a roentgenographic examination. The intensity for a given voltage and current is slightly lower with the high voltage rotating anode tube because of the increased inherent filtration. These intensities have been tabulated in milliroentgens per milliampere second at a distance of 1 meter for voltages from 50 kv. (peak) to 130 kv. (peak) and for added filtrations up to 3 mm. of aluminum (Tables I and II).

The half-value layers for the various conditions concerned are shown in Tables III and IV.

Table I

RADIATION INTENSITY USING A HIGH VOLTAGE ROTATING ANODE TUBE

| Filter | 50 | 60 | 70 | 85 | 100 | 130 |
|---|---|---|---|---|---|---|
| | Milliroentgens/Milliampere-Second at 1 Meter | | | | | |
| None | 7.6 | 10.2 | 13.3 | 18.4 | 22.5 | 29.6 |
| 0.5 mm. Al | 4.8 | 6.8 | 9.2 | 13.2 | 15.8 | 20.4 |
| 1.0 mm. Al | 3.2 | 4.6 | 6.3 | 9.6 | 12.0 | 15.9 |
| 2.0 mm. Al | 1.5 | 2.2 | 3.2 | 5.3 | 8.0 | 11.3 |
| 3.0 mm. Al | | | | 3.1 | 5.8 | 9.2 |

Table II

RADIATION INTENSITY USING A STATIONARY ANODE TUBE

| Filter | Kilovolts (Peak) | | | | |
|---|---|---|---|---|---|
| | 50 | 60 | 70 | 85 | 100 |
| | Milliroentgens/Milliampere-Second at 1 Meter | | | | |
| None | 8.2 | 11.6 | 14.9 | 19.8 | 25.0 |
| 0.5 mm. Al | 5.0 | 7.4 | 9.8 | 14.0 | 17.0 |
| 1.0 mm. Al | 3.3 | 4.8 | 6.7 | 10.0 | 12.8 |
| 2.0 mm. Al | 1.5 | 2.3 | 3.4 | 5.6 | 8.4 |
| 3.0 mm. Al | | | | 3.2 | 5.8 |

It is not possible to tabulate the intensity for any single distance and have it uniformly useful because of the wide variation in focal-skin distance, for in roentgenography the fixed distance is the focal-film distance and the focal-skin distance varies with the thickness of the part. The inverse square law can be used within practical limits to calculate the dose at other distances. For those who prefer to work in the English rather than the metric system, adequate calculations may be made using a factor of 40 inches instead of 1 meter.

The first thing that is readily apparent, of course, is that adding even small amounts of filtration reduces the dose rate by a large factor. Over the working voltage range for either tube 1 mm. of aluminum can be depended upon to reduce the dose by approximately 60 per cent, 2 mm. of aluminum by a factor of about 80

TABLE III

RADIATION QUALITY USING A HIGH VOLTAGE ROTATING ANODE TUBE

| Filter | Kilovolts (Peak) | | | | | |
|---|---|---|---|---|---|---|
| | 50 | 60 | 70 | 85 | 100 | 130 |
| | Half-Value Layer—mm. Al | | | | | |
| None | 0.75 | 0.83 | 0.88 | 0.91 | 1.00 | 1.20 |
| 0.5 mm. Al | 0.90 | 1.00 | 1.18 | 1.35 | 1.60 | 1.95 |
| 1.0 mm. Al | 1.05 | 1.25 | 1.40 | 1.54 | 1.95 | 2.90 |
| 2.0 mm. Al | 1.20 | 1.55 | 1.75 | 1.95 | 2.90 | 4.1 |
| 3.0 mm. Al | | | | 2.50 | 3.60 | 4.8 |

TABLE IV

RADIATION QUALITY USING A STATIONARY ANODE TUBE

| Filter | Kilovolts (Peak) | | | | |
|---|---|---|---|---|---|
| | 50 | 60 | 70 | 85 | 100 |
| | Half-Value Layer—mm. Al | | | | |
| None | 0.70 | 0.80 | 0.83 | 0.86 | 0.95 |
| 0.5 mm. Al | 0.85 | 0.96 | 1.15 | 1.31 | 1.57 |
| 1.0 mm. Al | 0.99 | 1.22 | 1.38 | 1.50 | 1.93 |
| 2.0 mm. Al | 1.18 | 1.53 | 1.75 | 1.92 | 2.91 |
| 3.0 mm. Al | | | | 2.48 | 3.60 |

per cent at 50 kv. (peak), about 70 per cent at 100 kv. (peak) and about 60 per cent at 130 kv. (peak).

How little the effect of added filtration of this order may have on the resulting roentgenogram will be apparent from what follows.

### TRANSMISSION THROUGH THE PART

The radiation that is transmitted through the part is the useful radiation in making the roentgenogram. In the light of present understanding the radiation that is not transmitted through the part can produce no useful effect. The aim should be to get as much of the total radiation through the part as is consistent with a satisfactory diagnostic film. For the information it might shed on this problem and on other problems of incidental nature, studies of the transmission through a phantom were made over the complete range of voltage and filtration. This information is reproduced in the form of curves for voltages of 50, 70, 85, 100 and 130 kv. (peak) in Figures 1, 2, 3, 4, 5.

It will quickly be noted that such curves resemble those taken in aluminum or copper for use in radiation therapy. There is considerable information to be had from these curves once one is accustomed to their use. The slope of the curve is a measure of contrast. The difference in level at any thickness is a measure of the relative exposure needed to make the roentgenogram.

All this points to a relatively low transmission at the voltages usually used for a given part thickness. The addition of filter increases the transmission by a large factor, at the same time reducing the incident dose. Only a very small portion of the incident radiation is used in making the roentgenogram. There would appear to

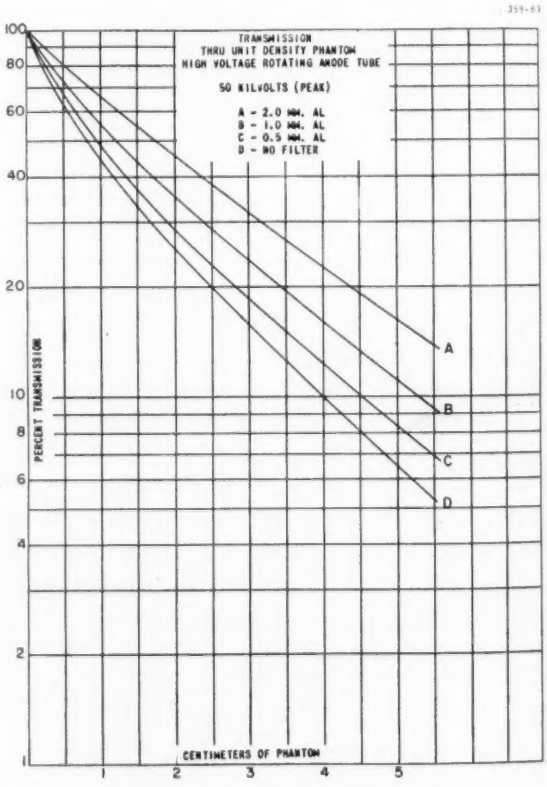


FIG. 1. Phantom transmission curves for 50 kv. (peak).

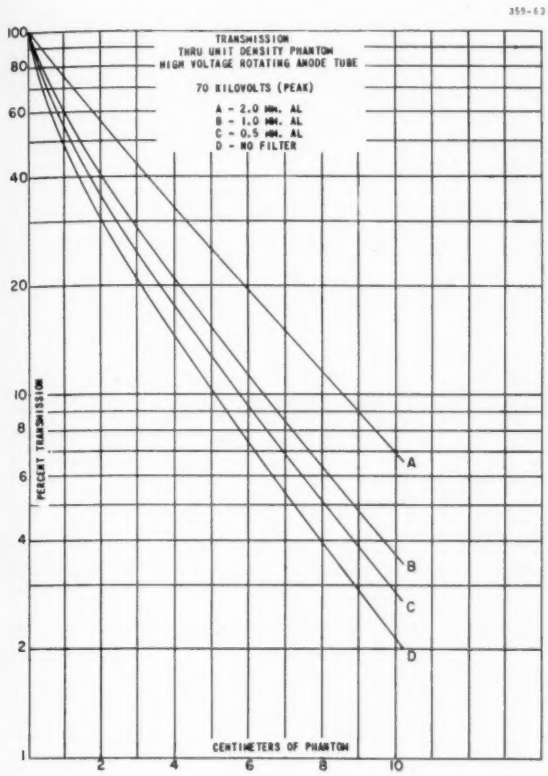


Fig. 2. Phantom transmission curves for 70 kv. (peak).

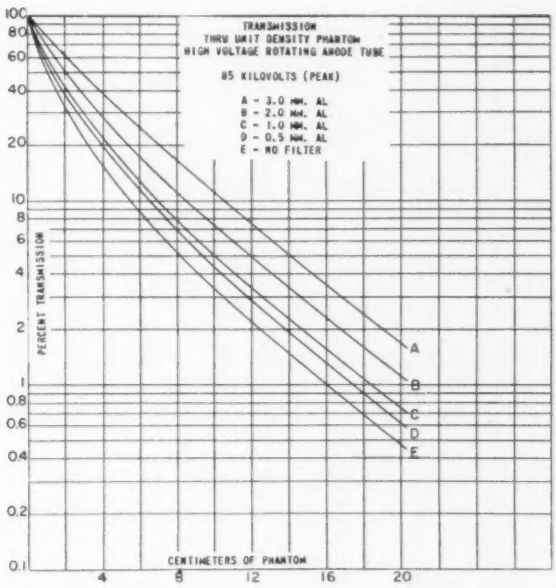


Fig. 3. Phantom transmission curves for 85 kv. (peak).

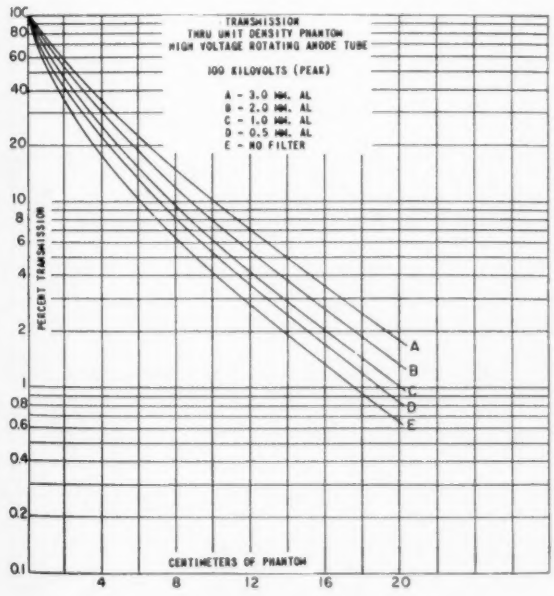


Fig. 4. Phantom transmission curves for 100 kv. (peak).

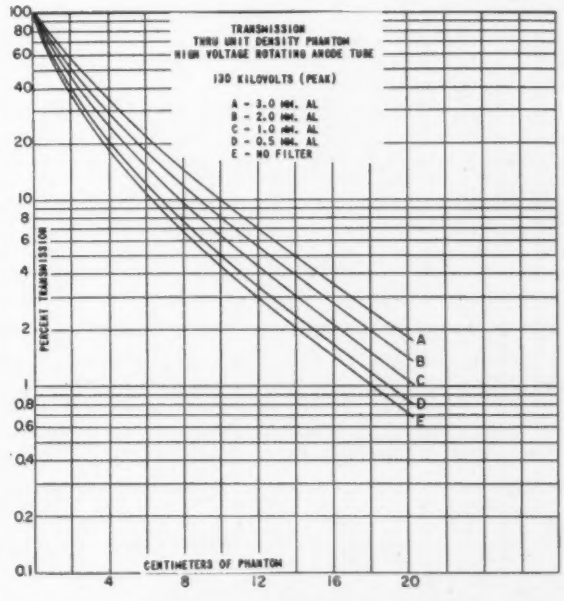


Fig. 5. Phantom transmission curves for 130 kv. (peak).

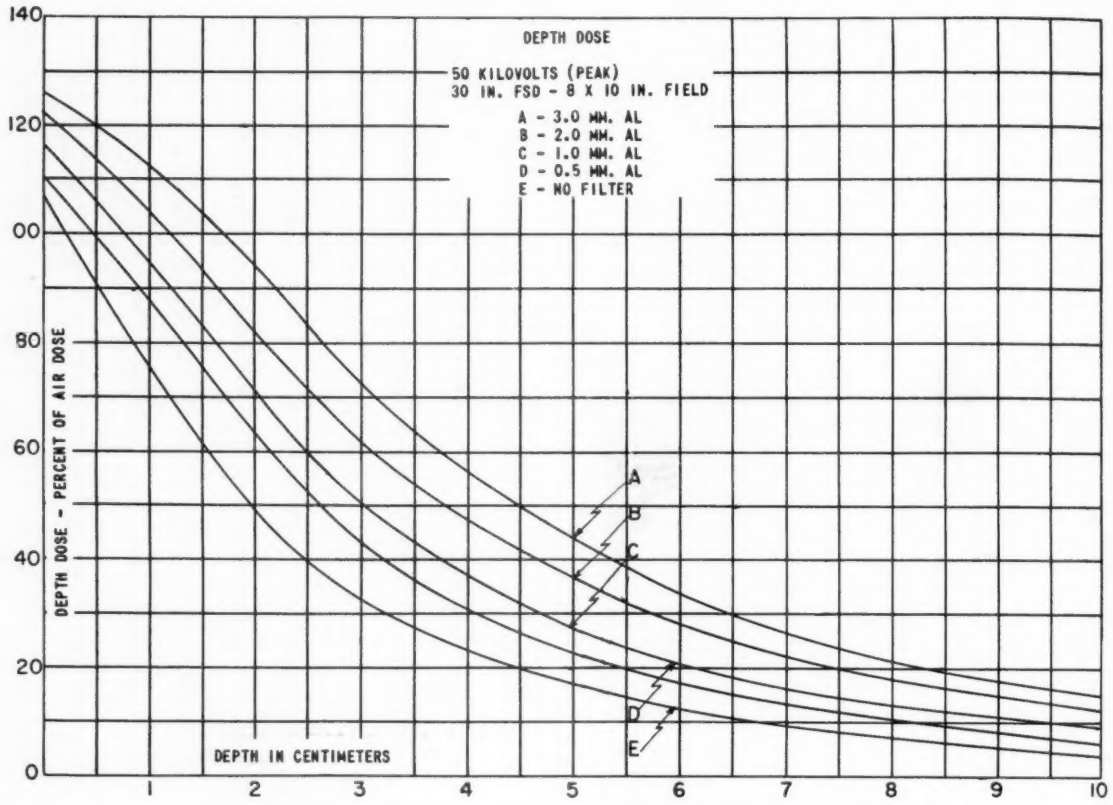


FIG. 6. Depth dose curves for 50 kv. (peak) 8 by 10 inch field.

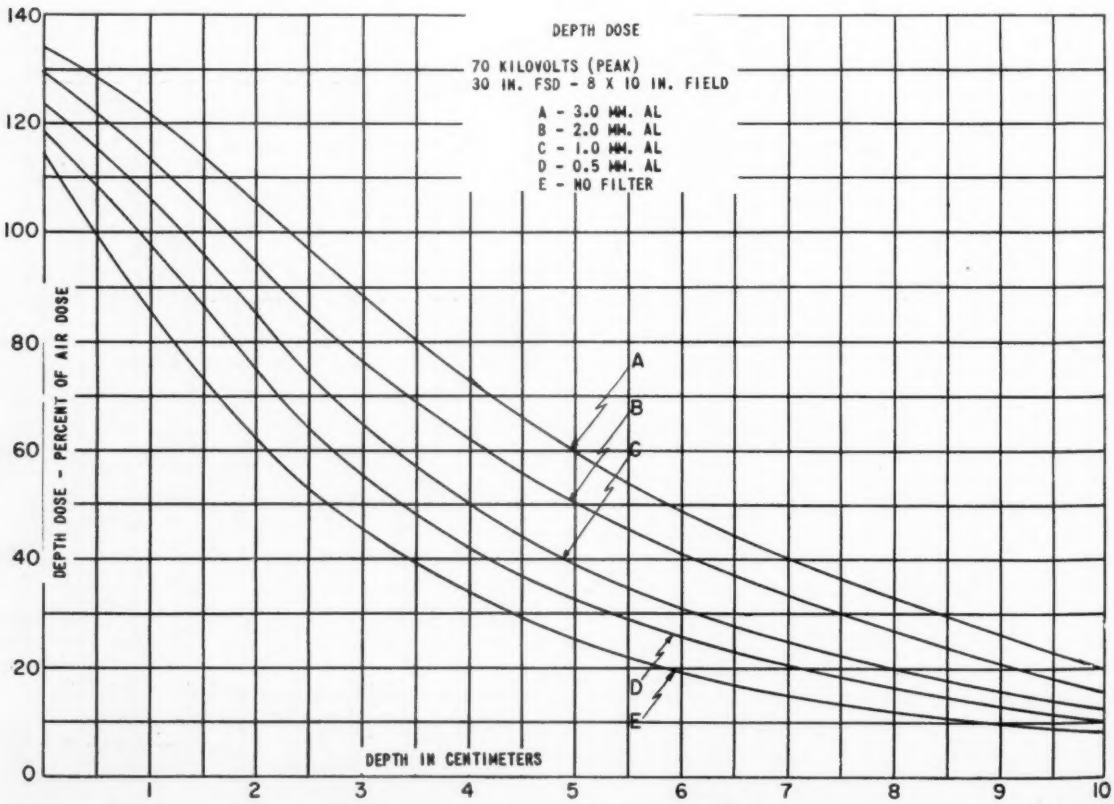


FIG. 7. Depth dose curves for 70 kv. (peak) 8 by 10 inch field.

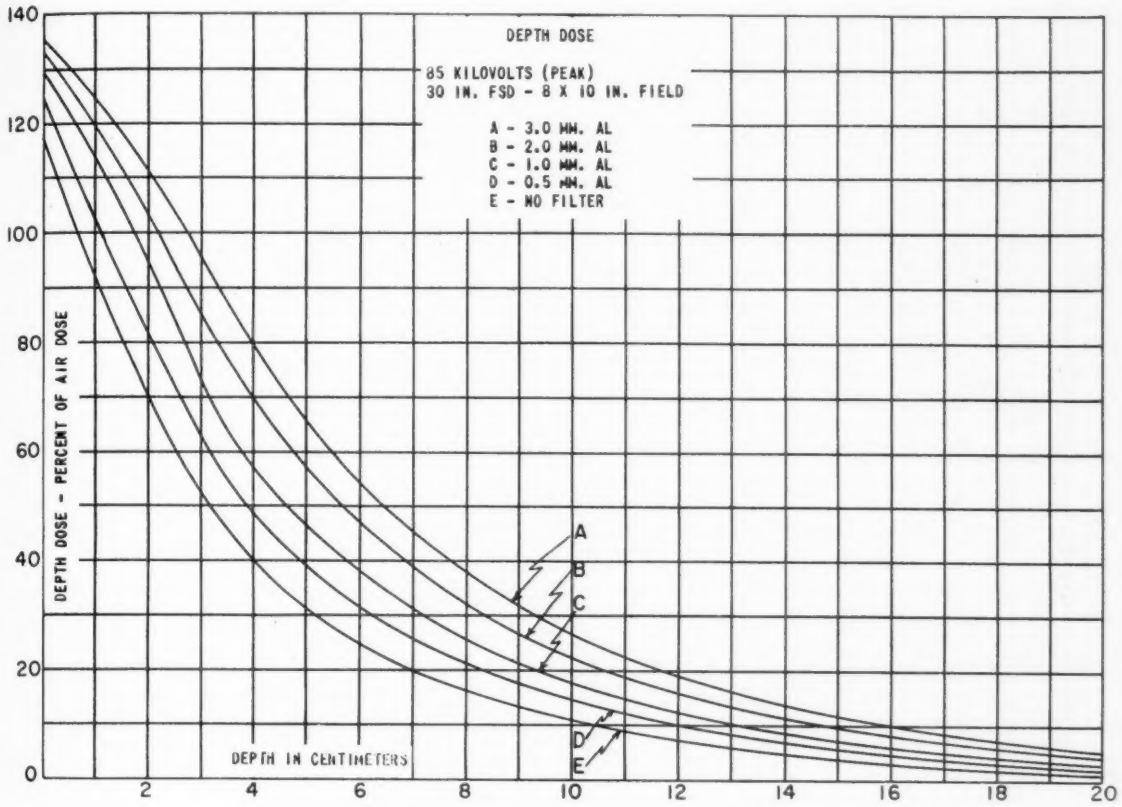


FIG. 8. Depth dose curves for 85 kv. (peak) 8 by 10 inch field.

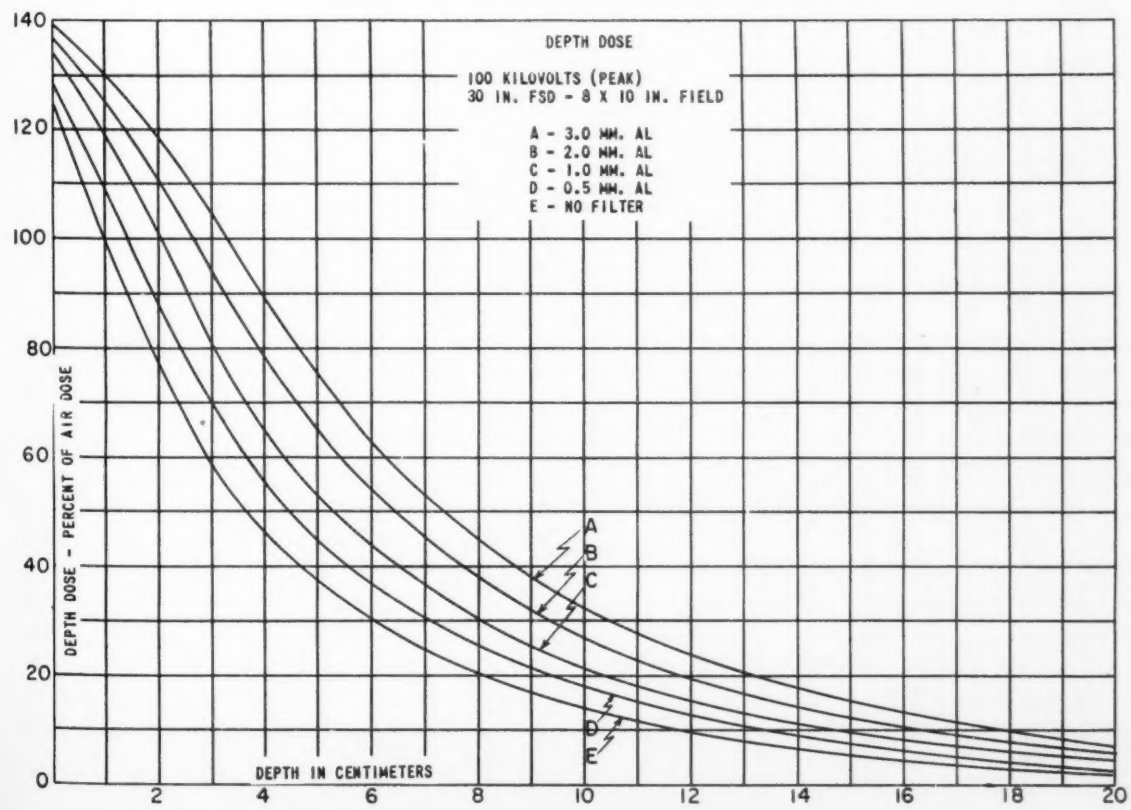


FIG. 9. Depth dose curves for 100 kv. (peak) 8 by 10 inch field.

be no reason why filtration could not be used to absorb some of the radiation that is absorbed by the part and which contributes nothing in the production of the roentgenogram. From the slope of these curves it would appear that the quality of the resulting roentgenogram would not be materially altered by the additional filtration. It would further seem that the increase in exposure time would not be in proportion to the decrease in the incident dose. Assuming that there is no change in the diagnostic quality of the roentgenogram, added filtration can be used to reduce the patient dose by absorbing much of the unused radiation.

### DEPTH DOSE

It is to be expected that the reduction in the incident dose and the increase in transmission would be accompanied by some change in the distribution of the radiation within the part. The soft radiation absorbed by the filters would lead to an increased percentage depth dose. It is not within the scope of these investigators to determine the influence of this in its long time effect on the patient. It was thought worthwhile, however, to include depth dose data for the use of those who may find it of significance.

Data of this kind readily available for use in roentgen therapy are of necessity restricted to higher voltages and smaller fields than those usually used in diagnostic procedures. Depth doses for an 8 by 10 inch field and a 14 by 17 inch field were determined at voltages of 50, 70, 85, 100 and 130 kv. (peak) (Fig. 6 to 15).

TABLE V

DOSE FACTORS FOR PELVIS ANTEROPOSTERIOR

Focal-Film Distance—40 inches
Focal-Skin Distance—30 inches

| Filter | Ma-Sec. | Skin Dose (in air) Milliroentgens | Dose in Milliroentgens at | | Transmitted Dose in Milliroentgens through Part |
|---|---|---|---|---|---|
| | | | 3 cm. | 9 cm. | |
| 60 kv. (peak) | | | | | |
| None | 141 | 2,380 | 1,060 | 227 | 24 |
| 0.5 mm. Al | 161 | 1,830 | 989 | 220 | 25 |
| 1.0 mm. Al | 164 | 1,260 | 793 | 206 | 26 |
| 3.0 mm. Al | 214 | 464 | 401 | 114 | 25 |
| 85 kv. (peak) | | | | | |
| None | 41 | 1,250 | 711 | 203 | 25 |
| 0.5 mm. Al | 41 | 860 | 576 | 190 | 26 |
| 1.0 mm. Al | 46 | 680 | 537 | 183 | 27 |
| 3.0 mm. Al | 55 | 290 | 302 | 113 | 26 |
| 130 kv. (peak) | | | | | |
| None | 12 | 593 | 409 | 148 | 29 |
| 1.0 mm. Al | 12 | 320 | 314 | 128 | 30 |
| 2.0 mm. Al | 12 | 227 | 254 | 109 | 29 |
| 3.0 mm. Al | 12 | 180 | 220 | 101 | 28 |

The procedure used in making these determinations varied from that used in taking therapy data in that a fixed phantom thickness was not always maintained below the chamber. The phantom thickness was fixed at the maximum and data taken by moving the chamber down in the phantom so that a decreasing phantom thickness resulted as the chamber was moved deeper into the phantom. The phantom was supported on a sheet of bakelite similar to that used in diagnostic tables so that at the maximum phantom

thickness there was still this piece of bakelite below the chamber. Over the range of voltages reported here, an increased phantom thickness below the chamber did not appear to produce a significant difference in the readings. At comparable qualities of radiation, the data obtained appear to be consistent with that found in roentgen therapy tables if the data are extrapolated to the field sizes in which we are interested.

In order to facilitate the use of the depth dose curves, the surface dose was plotted as the percentage of the air dose. With this and the preceding information it is possible to determine the incident dose, the depth dose, and the transmitted dose for diagnostic procedures. This has been done for pelvis roentgenograms taken on the same patient at 60, 85, and 130 kv. (peak) and is reproduced in Table v. This readily indicates the reduction in the skin dose and depth dose as the voltage and filtration are increased. The conclusion that can be drawn is that the highest voltage and thickest filter consistent with adequate contrast for diagnosis should always be used to reduce the patient dose. As the exit surface is approached, the depth dose approaches a constant value and at the table top is, within the limits of our measurements, a constant for any given voltage. This is to be expected if a constant film density is to be maintained. The influence of the grid on the exit radiation is now being studied since this will be reflected into the radiation that reaches the film. It must, of course, be borne in mind that this information is based on a phantom of homogeneous composition, a condition which does not prevail within the patient. Within the limits of experimental procedure, however, this is a condition which cannot be readily altered. Some idea of what occurs within a non-homogeneous part can be obtained from the excellent work of Spiers and of Wilson.

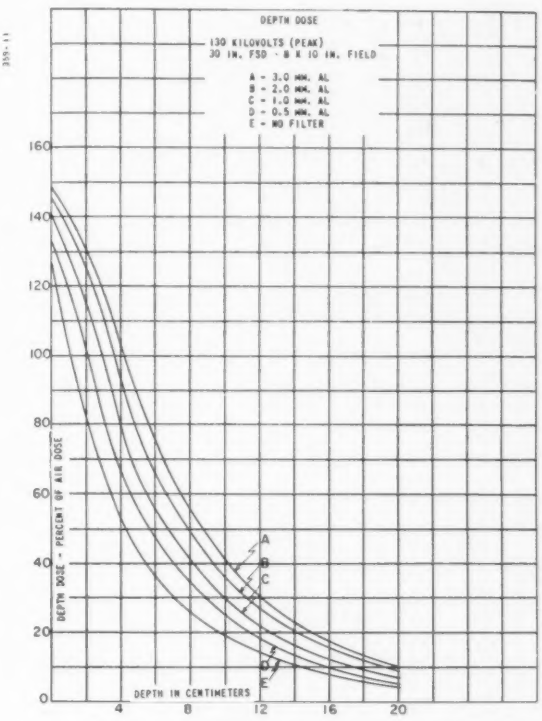


Fig. 10. Depth dose curves for 130 kv. (peak) 8 by 10 inch field.

## ROENTGENOGRAMS

Roentgenograms were made of parts ranging from the lateral elbow to the lateral lumbar spine. Within its working range, the phototimer was used to bring the films to uniform density as filter was added. From the cycle counter it was possible to determine the exposure time and thus compute the exposure in milliampere-seconds and by both direct measurement and computation the dose reaching the skin of the patient. Tables showing these factors for various parts were prepared. From these tables it will be seen that the dose is reduced by a much greater factor than the increase in exposure time as filter is added. It will also be seen that increased voltage reduces the patient dose (Tables vi to x).

It is difficult to appraise the diagnostic value of a roentgenogram from slides or printed reproductions. The best that can be done is to photograph a complete series of roentgenograms simultaneously and this has been done to produce Figures 16, 17 and 18.

From these reproductions it may be noted that there is virtually no difference in the quality of the roentgenograms for

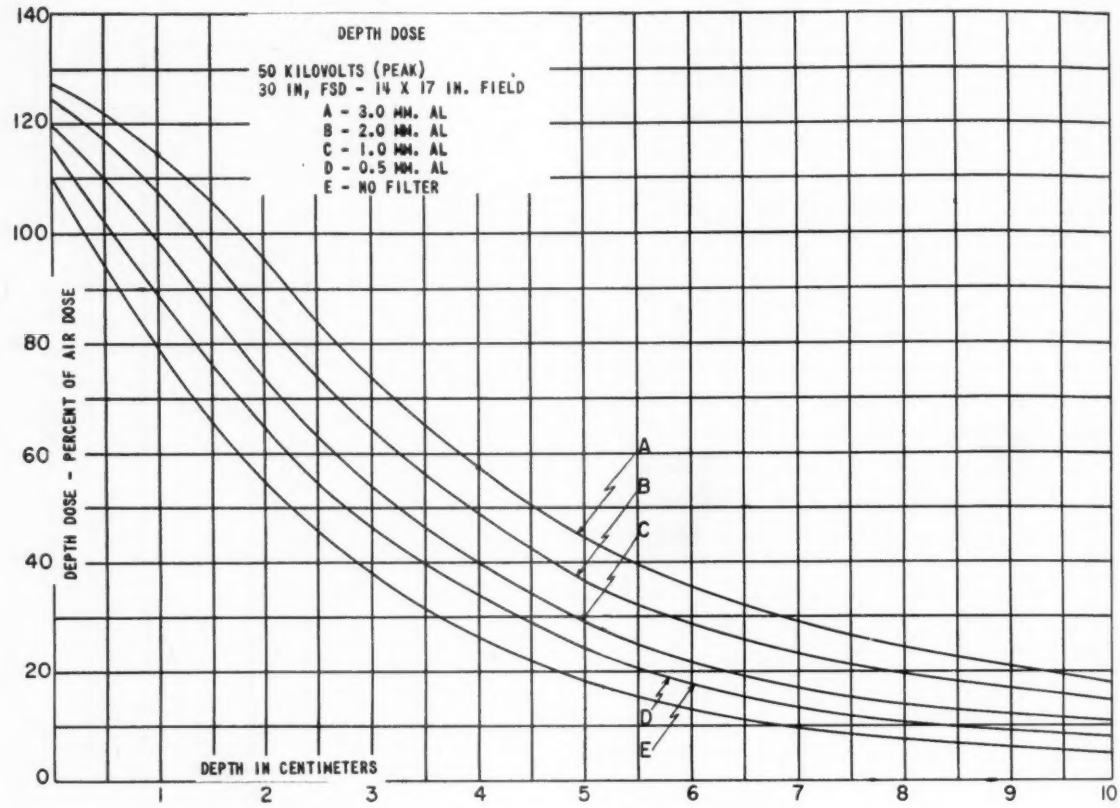


FIG. 11. Depth dose curves for 50 kv. (peak) 14 by 17 inch field.

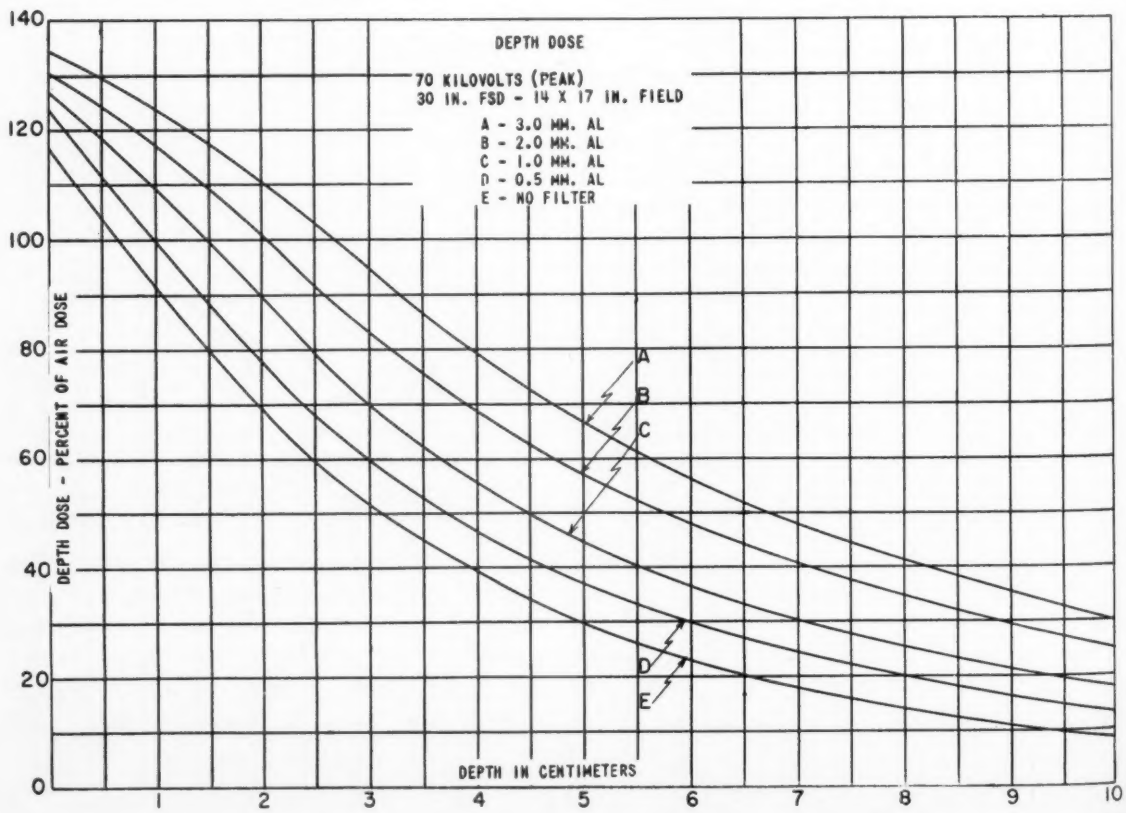


FIG. 12. Depth dose curves for 70 kv. (peak) 14 by 17 inch field.

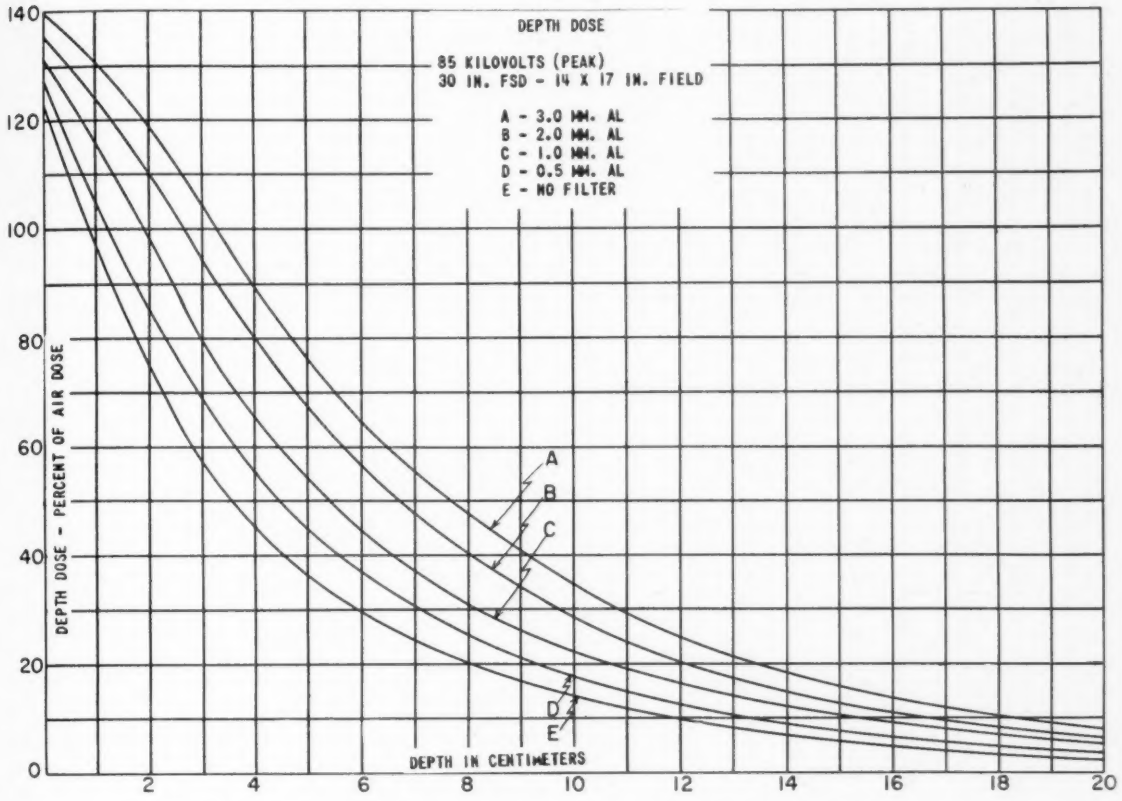


Fig. 13. Depth dose curves for 85 kv. (peak) 14 by 17 inch field.

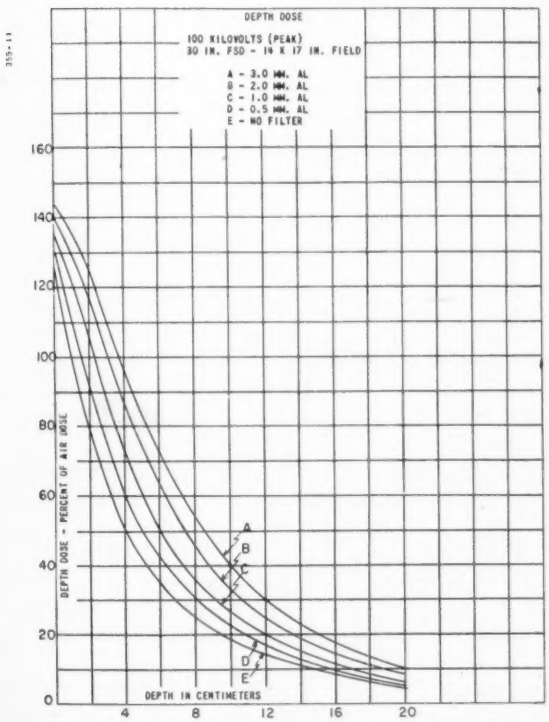


Fig. 14. Depth dose curves for 100 kv. (peak) 14 by 17 inch field.

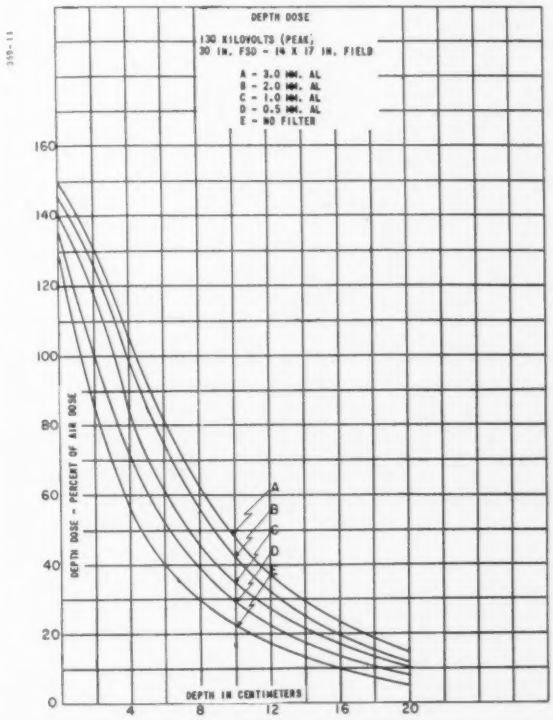


Fig. 15. Depth dose curves for 130 kv. (peak) 14 by 17 inch field.

added filtrations up to 2 mm. of aluminum at voltages up to 70 kv. (peak); above 70 kv. (peak) 3 mm. of aluminum (or 0.1 mm. of copper) produces no significant changes in the roentgenogram. At 130 kv. (peak) and thick parts even 0.25 mm. of copper does not appear to alter the roentgenogram. In the higher voltage range, the phototimer cannot detect the addition of 0.5 mm. of aluminum. At 130 kv. (peak) filtration up to 2 or 3 mm. of aluminum can be added without any change in exposure time.

Before starting this work there was some fear that increased filtration might either alter the contrast of the roentgenogram or bring about an undesirable result by reducing the density of the unprotected portion of the film. Thus far, neither of these difficulties has been encountered. A review of roentgenograms made fifteen or more years ago does show that in the case of chest roentgenography as little as 1 mm. of aluminum produced a marked decrease in

TABLE VI

COMPARATIVE EXPOSURE
PELVIS
60 kv. (peak), 40 inch focal-film distance, 18 cm. patient

| Filter | Milli-ampere-Seconds | Factor | Skin Dose (in air) Milli-roentgens | Factor |
|---|---|---|---|---|
| None | 141 | 1.00 | 2,380 | 1.00 |
| 0.5 mm. Al | 161 | 1.14 | 1,850 | 0.78 |
| 1.0 mm. Al | 164 | 1.17 | 1,270 | 0.53 |
| 3.0 mm. Al | 214 | 1.52 | 465 | 0.20 |

TABLE VII

COMPARATIVE EXPOSURE
PELVIS
85 kv. (peak), 40 inch focal-film distance, 18 cm. patient

| Filter | Milli-ampere-Seconds | Factor | Skin Dose (in air) Milli-roentgens | Factor |
|---|---|---|---|---|
| None | 41 | 1.00 | 1,225 | 1.00 |
| 0.5 mm. Al | 41 | 1.00 | 860 | 0.70 |
| 1.0 mm. Al | 46 | 1.12 | 684 | 0.56 |
| 3.0 mm. Al | 55 | 1.34 | 287 | 0.23 |

TABLE VIII

COMPARATIVE EXPOSURE
PELVIS
130 kv. (peak), 40 inch focal-film distance, 18 cm. patient

| Filter | Milli-ampere-Seconds | Factor | Skin Dose (in air) Milli-roentgens | Factor |
|---|---|---|---|---|
| None | 12 | 1.00 | 590 | 1.00 |
| 1.0 mm. Al | 12 | 1.00 | 324 | 0.54 |
| 2.0 mm. Al | 12 | 1.00 | 230 | 0.39 |
| 0.1 mm. Cu | 12 | 1.00 | 170 | 0.28 |
| 0.25 mm. Cu | 12 | 1.00 | 91 | 0.15 |

TABLE IX

COMPARATIVE EXPOSURE
LATERAL LUMBAR SPINE
85 kv. (peak), 40 inch focal-film distance, 23 cm. patient

| Filter | Milli-ampere-Seconds | Factor | Skin Dose (in air) Milli-roentgens | Factor |
|---|---|---|---|---|
| None | 72 | 1.00 | 2,450 | 1.00 |
| 0.5 mm. Al | 72 | 1.00 | 1,720 | 0.70 |
| 1.0 mm. Al | 76 | 1.06 | 1,290 | 0.53 |
| 3.0 mm. Al | 89 | 1.23 | 526 | 0.22 |

TABLE X

COMPARATIVE EXPOSURE
LATERAL LUMBAR SPINE
130 kv. (peak), 40 inch focal-film distance, 23 cm. patient

| Filter | Milli-ampere-Seconds | Factor | Skin Dose (in air) Milli-roentgens | Factor |
|---|---|---|---|---|
| None | 16 | 1.00 | 895 | 1.00 |
| 1.0 mm. Al | 17 | 1.06 | 538 | 0.60 |
| 2.0 mm. Al | 18.5 | 1.15 | 404 | 0.45 |
| 0.1 mm. Cu | 20 | 1.25 | 321 | 0.35 |

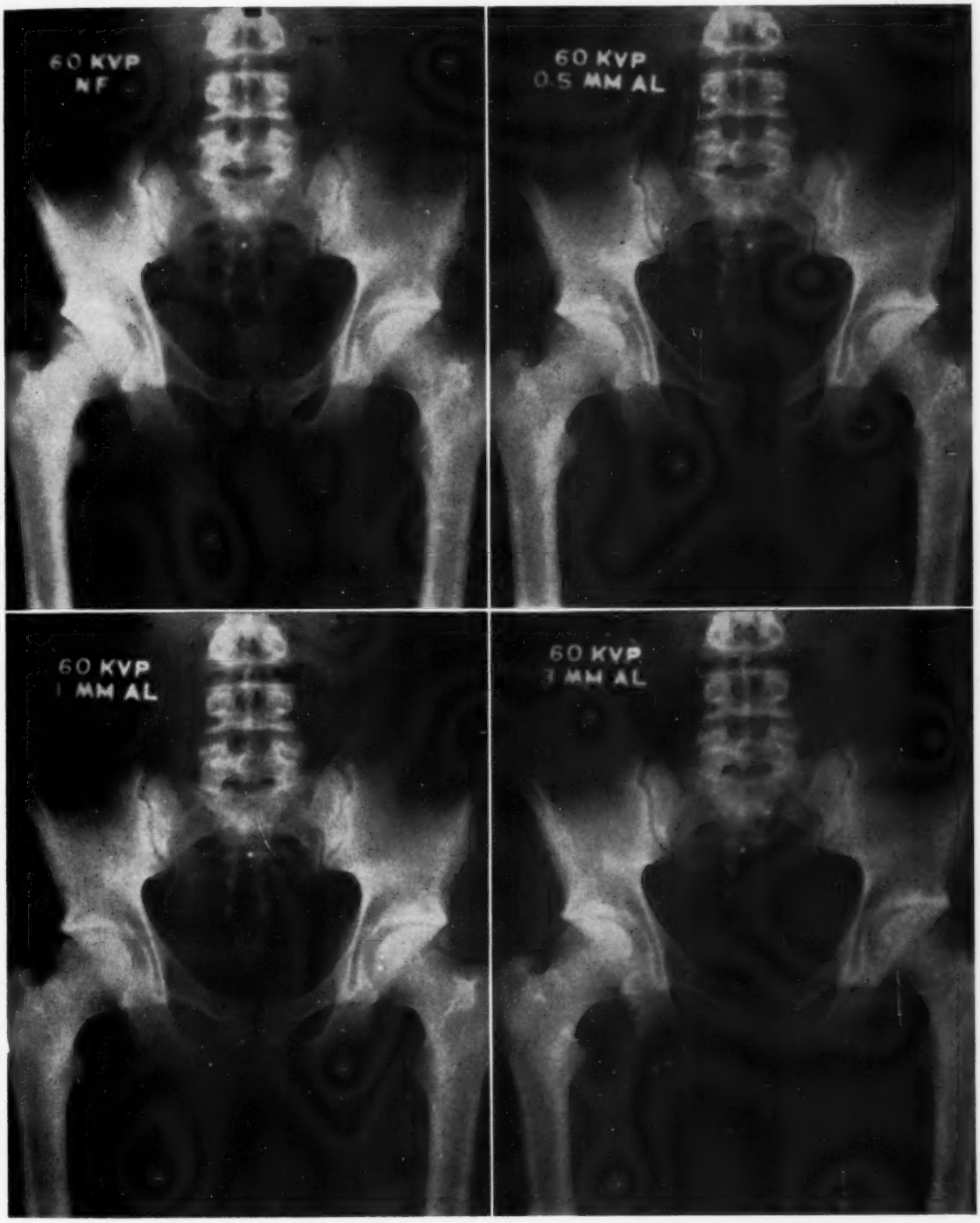


Fig. 16. Anteroposterior views of pelvis. Roentgenograms taken at 60 kv. (peak), no filter to 3.0 mm. Al.

the density of the unprotected portion of the film. This does not presently appear to be true. It is believed that improvement in film emulsions might have brought this about. Some of the emulsion characteristics necessary for high quality industrial roentgenography appears to have been reflected into modern medical emulsion techniques.

In addition to roentgenograms of patients, a series of exposures was made

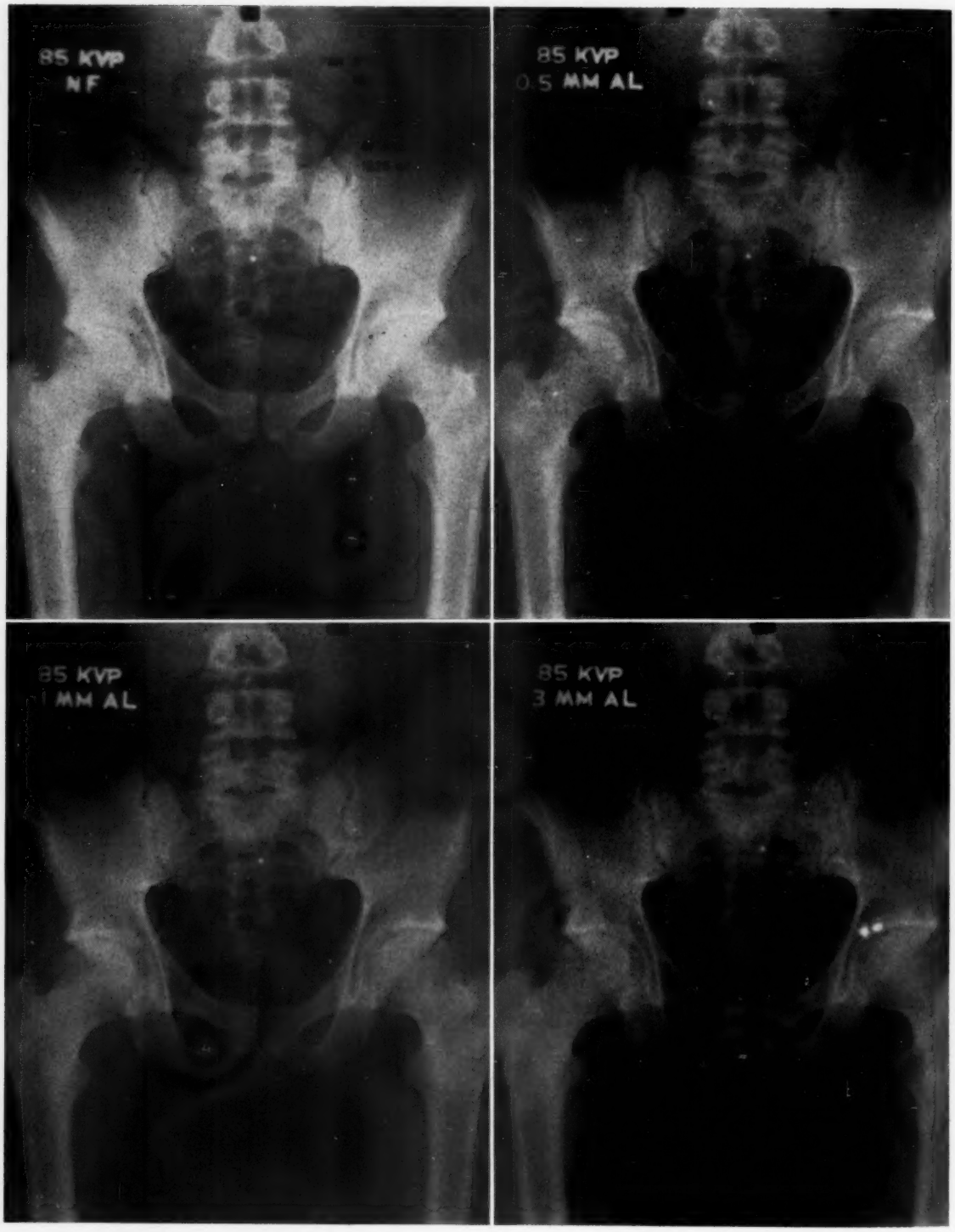


FIG. 17. Anteroposterior views of pelvis. Roentgenograms taken at 85 kv. (peak), no filter to 3.0 mm. Al.

using an aluminum step-block similar to that widely used in roentgenographic calibration. A plot of the film density for the various section thicknesses with the filters and voltages used indicates how little the density varies over a wide range

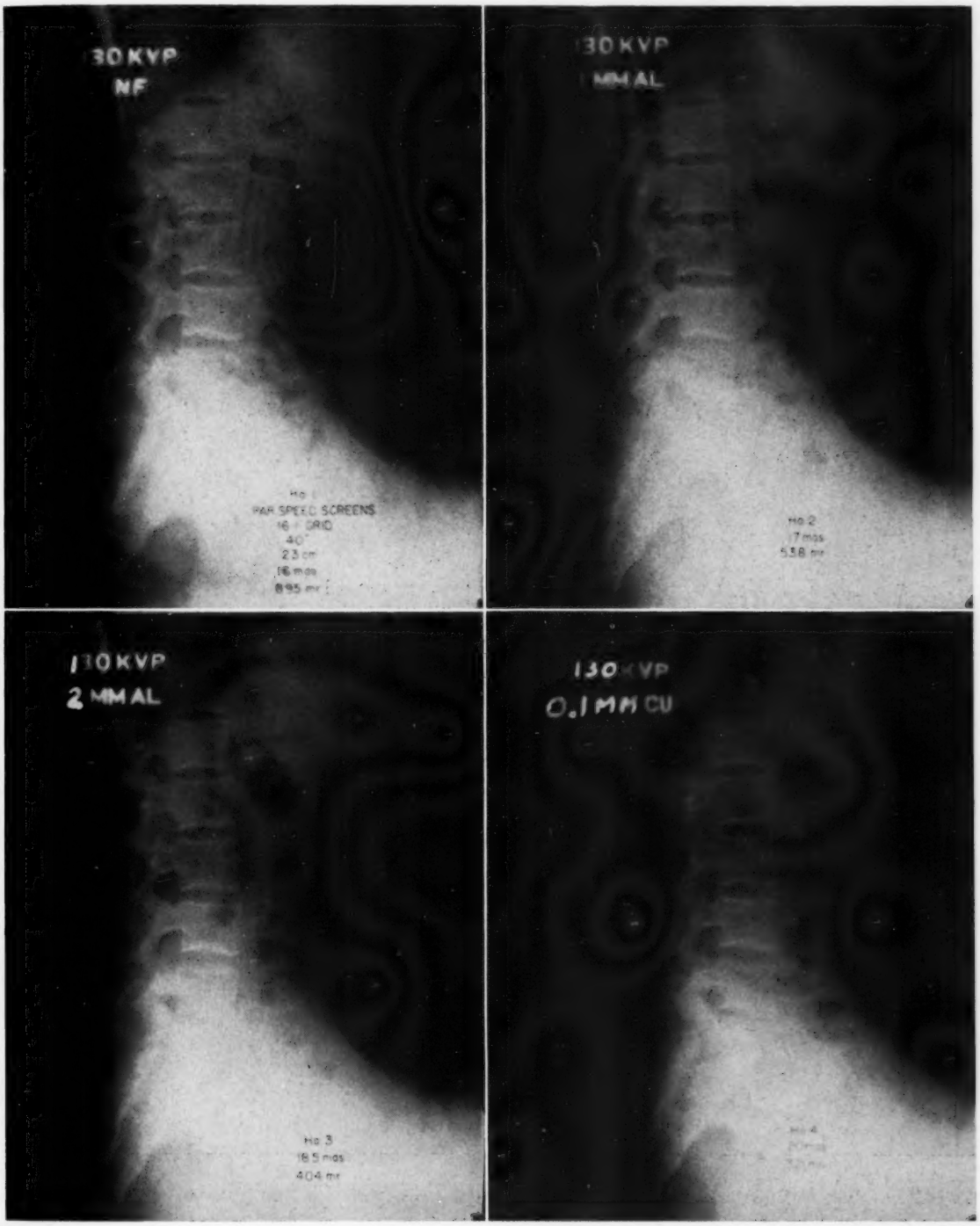


Fig. 18. Lateral views of lumbar spine. Roentgenograms taken at 130 kv. (peak), no filter to 0.1 mm. Cu.

of thicknesses when the exposure is controlled to bring about a uniform density for one of the middle thicknesses (20 mm.) (Fig. 19).

In pregnancy examinations there may be special reason to reduce the patient dose to a minimum. To determine the doses involved and to test our conclusions as to the ease with which filters could be used, we asked Drs. House and Clarke of

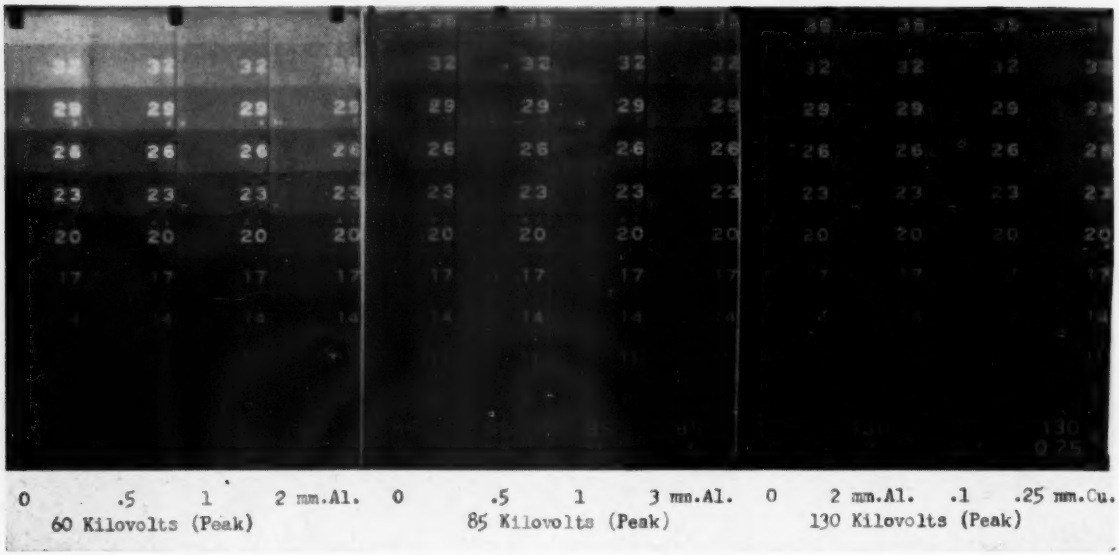


FIG. 19. Aluminum stepblock roentgenograms for 60, 85 and 130 kv. (peak).

Oneonta, New York, to make a series of exposures at 100 kv. (peak) using no filter, 1, 2, and 3 mm. of aluminum without any change in technique on the next such examination done by them. The resulting roentgenograms reproduced in Figure 20 show no significant differences in the first three films. The one made using the 3 mm. filter is slightly reduced in density although the variation throughout the series is not greater than that usually encountered in the course of a day's work in many hospitals. An increase of 20 per cent in exposure time would have brought the film density up to that of the other roentgenograms. An analysis of the factors involved is shown in Table XI.

## CONCLUSION

In conclusion, we would say—use 2 mm. aluminum at voltages from 50 to 70 kv. (peak), use 3 mm. aluminum at voltages above 70 kv. (peak), and up to 0.25 mm. copper above 100 kv. (peak). Use the highest voltage consistent with the contrast needed for diagnosis. And, finally, let us take as our creed this quotation from the preface to the National Bureau of Standards Handbook 41: "With the increasing use of radiation and of materials emitting

TABLE XI

DOSE FACTORS FOR PREGNANCY EXAMINATION

Focal-Film Distance—40 inches
Focal-Skin Distance—29 inches

| Filter | Ma-Sec. | Skin Dose (in air) Milliroentgens | Dose in Milliroentgens at | | Transmitted Dose in Milliroentgens through Part |
|---|---|---|---|---|---|
| | | | 3 cm. | 9 cm. | |
| 100 kv. (peak) | | | | | |
| None | 40 | 475 | 292 | 100 | 12 |
| 1.0 mm. Al | 40 | 253 | 222 | 76 | 12 |
| 2.0 mm. Al | 40 | 169 | 172 | 64 | 11 |
| 3.0 mm. Al | 40 | 122 | 135 | 56 | 10 |

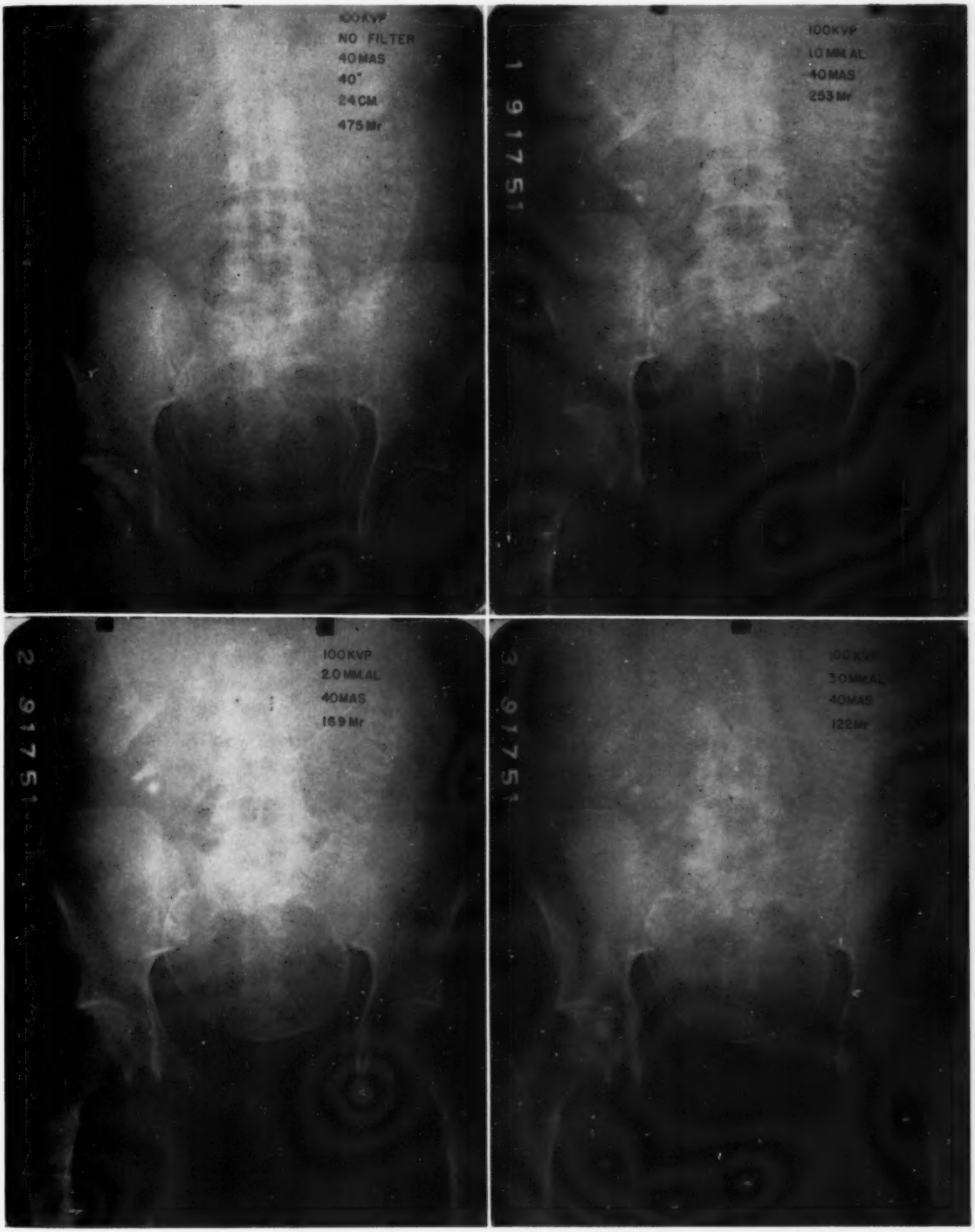


Fig. 20. Pregnancy roentgenograms; 100 kv. (peak), no filter to 3.0 mm. Al.

radiation, it is necessary for the medical profession to exercise great caution and restraint in the use of x-rays for diagnosis and the treatment of non-malignant diseases. Current methods and practices should be reviewed to see whether the same result could be obtained with less radiation."

The authors are indebted to Drs. LeRoy House and John Clarke for their help in providing the pregnancy roentgenograms; and to the many roentgenologists and radiation physicists whose advice and suggestions have aided and guided us in this work.

4855 Electric Ave.
Milwaukee 14, Wisconsin

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DISCUSSION

DR. F. O. COE, Washington, D. C. This is a very timely subject. The study was well conceived and excellently executed. It is especially timely as we are being warned by our insurance companies and by other sources of the problems of lawsuits against the medical profession. This is a peculiar way to approach this problem. Today the persons who have not are trying to get. The population in general is being informed of the effects of radiation not "x-ray burns" or "erythema doses" but the "effects on $F_1$ and $F_2$ generations."

The details of the subject have been well covered by the essayists. I have not seen any recent accidents in the way of excessive radiation from roentgenographic studies, and we are not so much concerned with immediate results of radiation but the effects on the male and female gonads. Dr. Ramsey Spillman called our attention to this a long time ago with so much emphasis that it seemed risky to make an exposure of the pelvis of either a male or female. Because of my work on pelvimetry I am sure that the subject presented is well taken and I will institute the use of filters.

It has been proved to my satisfaction from carefully studying the original films which Mr. Trout presented that it is impossible to see any change in the diagnostic properties of the roentgenograms of all of the parts of the body taken with the exception of the chest. The addition of filters in the taking of the chest reduced the density of the film and thus the contrast areas, though the detail was well seen.

Dr. Trout has indicated that the addition of 2 mm. of aluminum is about correct for intermediate voltages. He suggests that we go to 3 mm. for the higher voltages. I am not ready to concur in this until a trial has been made. Two millimeters reduced the dosage on the skin to about one-third. The reduction was as high as 66 per cent in some cases and of course there is a corresponding difference in the depth dose.

One thing I would like to have the essayist do is to present this matter in a simplified form that can be easily explained to the tech-

nicians. Technicians are making most of the roentgenographic exposures in our office and I believe they are doing the same throughout the country. We cannot make most of the exposures as we once did. Many radiologists who do not have a large number of roentgenographic units will have to be changing filters quite frequently for different voltages. I will immediately institute the use of 2 mm. of aluminum in all of the roentgenographic work of the torso except the chest. This is especially necessary in pelvimetric studies and views of the gastrointestinal tract.

This subject is presented at a time which seems a longer period from the earlier days in which adequate filters were used. With the institution of the Potter-Bucky diaphragm, roentgenographic exposures were made on a shotgun plane instead of using a rifle as in the early days with small cones. Adequate filters were used with the gas tubes. It is time that we followed the suggestion of Mr. Trout and for numerous reasons institute the use of filters.

Miss Lillian E. Jacobson, New York, New York. I wonder how many private offices are adequately protected for this quality of radiation insofar as secretaries, technicians, and others are concerned. We think in terms of protection of the patient; the people working in the offices are there all day and the penetration of this radiation is greater than that for which the office and tube housing have been designed.

Dr. Robert R. Newell, San Francisco, California. It is awfully hard to get rid of the old superstititon that the lower the voltage, the brighter the picture and the more you can see in it. I don't know of very many injuries to patients by diagnostic radiation except through gross carelessness, but we are getting more sensitive all the time to the possibility of remote effects from radiation injuries and we ought to be watching out to reduce the amount of roentgen radiation that we give our patients everywhere we can, even small amounts. It is quite clear that these filters removed two-thirds or three-quarters of the roentgen radiation that reached the patient, but they only removed one-sixth of the roentgen radiation that reached the film. Surely one is willing to pay a price of one-sixth in order to save the patient three-quarters.

In regard to the chest, it is not hard to show that you can actually do a better job of seeing fuzzy, faint infiltrations in the lungs if you will use 100 kv. with 3 mm. of aluminum filter than you can at any softer quality. Our prejudice in favor of low voltage is not only inefficient and bad for the patients, but it also does injury to our diagnostic acumen. We will do better in looking for pulmonary lesions to use high voltage and a filter.

Dr. E. T. Leddy, Rochester, Minnesota. For a long time I have been interested in injuries resulting from roentgenologic diagnostic procedures and I have written about some of the ways in which they might be prevented. The presentation by Dr. Trout of their method of producing roentgenograms by a precision technique in which high voltage and filtration are used is, it seems to me, a noteworthy step toward greater safety and therefore one that merits prompt adoption.

Dr. Trout (closing). In answer to Dr. Jacobson's query, I think there may be a solution to that problem. Dr. Braestrup is in the audience and he has done more on this than anybody I know and I think could probably answer it much more factually and much more readily. I have the feeling that, due to the fact that when the higher voltage is used, the exposures are so much shorter, in the long run the total dose of scattered radiation at the technician's position may not be as much as we might assume.

I know nothing about it for we have made no attempt to analyze it. Protection around diagnostic installations until recently was based on about 85 or 100 kv. as recommended in Handbook 20.

Dr. Newell has a very interesting paper on the subject that he mentioned here, the use of filters in chest work. I heard his paper in Denver; it is an excellent presentation and scientifically sound.

# DIRECT IRRADIATION OF CARCINOMA OF THE LIVER AND BILIARY TRACT BY THE USE OF RADIOACTIVE IODINE ($I^{131}$) IN TETRAIODOPHENOLPHTHALEIN*

## AN EXPERIMENTAL AND CLINICAL STUDY

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CARCINOMA of the liver, primary and secondary, and of the extrahepatic biliary tract is usually not amenable to surgical removal, nor have these malignancies responded satisfactorily to external radiation therapy. Malignancy of the biliary tract, therefore, has a uniformly bad prognosis. It occurred to us that the use of radioactive isotopes as sources of direct radiation might prove to be more highly specific than radiation therapy by means of exposure to roentgen rays or implantation of radium. We believed it would be possible to selectively irradiate the liver and the extrahepatic biliary system with tetraiodophenolphthalein containing radioactive iodine ($I^{131}$). The concentration of tetraiodophenolphthalein in the gallbladder for use in cholecystography was discovered by Graham and Cole.[1] The use of such a compound of radioactive tetraiodophenolphthalein would give the opportunity to observe the effect of beta and gamma radiations it emitted on normal and malignant tissue within the body, as well as on the bile, blood and urine.

A compound of tetraiodophenolphthalein was prepared by one of us (V.H.W.) in which radioactive iodine ($I^{131}$) was incorporated. The radioactive iodine was obtained from the Clinton Laboratories at Oak Ridge, Tennessee. With one exception, the iodine obtained from Oak Ridge had been freed from the bulk of tellurium and was in the form of an aqueous solution of sodium iodide. From May 5, 1947, to July 1, 1948, twenty-five chemical runs were made, incorporating in each instance about 35 millicuries of iodine 131 into about 3.5 gm. of sodium tetraiodophenolphthalein. There was minimal decay during transit of the $I^{131}$ whose half-life is eight days. Protection against radiation hazards was maintained at all times.

*Procedure Used in Production of Radioactive Sodium Tetraiodophenolphthalein.* In outline, the procedure consisted in (1) liberation and extraction of free iodine from the solution as received from Oak Ridge. This was accomplished by acidification, oxidation by sodium nitrite and then extraction by carbon tetrachloride. The radioactive iodine was extracted from the carbon tetrachloride by sodium hydroxide and, after acidification, was mixed with the main quantity of ordinary iodine monochloride used for iodination; (2) iodination of a freshly precipitated mixture of phenolphthalein and tetraiodophenolphthalein by stirring with the iodine monochloride mixture containing the radioactive iodine; (3) purification and solution of the product.

For the extraction there were used two 125 milliliter separatory funnels with glass stoppers on a suitable rack. The iodination vessel consisted of a 200 cc. 3 neck flask fitted in the center opening with a glass stirrer driven by a variable speed motor. One of the side openings

* We are indebted to Martin D. Kamen, Ph.D. for aid in making the dosage calculations given in this paper.

† Formerly of the Mallinckrodt Institute of Radiology, St. Louis; now at Seton Hospital, Austin, Texas.

was provided with a thermometer, the other being used for charging and sampling. Rubber stoppers were used. The flask, during the reaction, was vented only through the glass tube used as a bearing for the stirrer. For filtrations and preparing the final solution two ordinary 500 cc. suction flasks were used with a sintered glass filter (pyrex "F" grade) of about 50 ml. capacity. There was provided a wash bottle with rubber extensions so that it could be used without the operator's face being close to the point of application.

Distilled water for making up the final product was prepared by charging the still with about 700 ml. of distilled water and 0.5 gm. $KMnO_4$. The first 200 ml. of distillate was rejected, after which 150 ml. was collected for use and stored in a sterilized 500 ml. Erlenmeyer flask plugged with cotton. If not used immediately, it was stored not longer than one day in the refrigerator.

Special reagents required were:

Tetraiodophenolphthalein
Phenolphthalein
Sodium hydroxide solution 35° Baumé (38 per cent wt. vol.)
Concentrated hydrochloric acid (36 per cent HCl by weight)
10 per cent hydrochloric acid
N/1 sodium hydroxide
N/1 hydrochloric acid
Sodium bisulfite
Carbon tetrachloride analytical reagent
Sodium iodide solution (.005 gm/ml.)
Dilute sulfuric acid (10 per cent)
1 per cent sodium nitrite solution
Iodine monochloride—the material used contained 5 per cent by weight of concentrated hydrochloric acid to keep it liquid at room temperature. It contained approximately 94.5 per cent iodine monochloride by weight
Dilute acetic acid (1:5)
Dilute acetic acid (1:20)

The following pieces of equipment were wrapped in towels and sterilized in the pressure autoclave preparatory to each run:

1—500 ml. suction flask
The sintered glass funnel (mentioned above) with attached stopper
1—100 ml. graduated cylinder
1—500 cc. Erlenmeyer flask, plugged with cotton (but not wrapped)
1—Screw cap bottle—85 ml. or more capacity for the final product.

The following is a description of a typical run: The shipment of radioactive iodine contained 50 millicuries in 13.2 ml. but 0.3 cc. had been removed for test purposes. At 3:30 P.M. November 20, 1947, it measured 0.60 r/8 hr. at a distance of 18 inches.

In the stirred flask a mixture of 1.130 gm. of phenolphthalein and 0.735 gm. of tetraiodophenolphthalein was dissolved in 20 ml. of water by the addition of 1.0 ml. of sodium hydroxide 35° Baumé. Then 4.5 ml. of dilute hydrochloric acid (10 per cent) was added to precipitate the phthaleins. After fifteen minutes' stirring, the mixture was allowed to stand until needed.

Into one of the separatory funnels was added 10 ml. of carbon tetrachloride, 0.2 ml. sodium iodide solution (0.005 gm/ml.) and 2 ml. of 1 per cent sodium nitrite solution. The radioactive iodine solution was then poured into the funnel, rinsing out the bottle with enough distilled water to make the total water phase about 50 ml. There was then added 2.0 ml. of dilute sulfuric acid (10 per cent) and the funnel was closed and shaken vigorously by hand for ten to fifteen seconds. After a few minutes the carbon tetrachloride was drawn off into the other funnel. Ten milliliters more carbon tetrachloride was added to the first funnel and the extraction repeated until a total of four extractions had been made. The aqueous liquid in the first funnel was drawn off into a bottle labeled "First liquor after extraction." The combined carbon tetrachloride extracts in the second separatory funnel were treated with 10 ml. of water and 1.5 ml. of N/1 sodium hydroxide, shaken vigorously for ten to fifteen seconds and allowed to settle about ten minutes. The carbon tetrachloride layer was then drawn off into a bottle labeled "Washed carbon tetrachloride." Meanwhile there was prepared a solution of 0.92 ml. of iodine monochloride in 1 ml. of concentrated hydrochloric acid. The solution in the funnel was acidified with 2.0 ml. of N/1 hydrochloric acid. The iodine monochloride solution was then added and the combined solution was drained immediately into the flask containing the precipitated phthaleins and the funnel was rinsed, using the wash bottle. The flask was closed with a rubber stopper and the mixture was stirred gently at room temperature from 6:30 P.M. until the next morning.

At 8:00 o'clock the next morning 0.5 gm. of sodium bisulfite was added to the mixture. The crude tetraiodophenolphthalein was dissolved by the addition of 7.0 ml. of 35° Baumé

sodium hydroxide and reprecipitated by 7.5 ml. of dilute (1:5) acetic acid. The mixture was stirred thirty minutes at 70–90° C. to coagulate the tetraiodophenolphthalein, which was filtered by suction on the sintered glass funnel and washed several times with distilled water. The liquors were bottled and labeled "Mother liquor from T. I. P." The funnel, together with the solid, was fitted to the sterilized suction flask and, without any suction being applied, the solid was dissolved in the funnel by adding 40 ml. of the specially redistilled water and N/1 sodium hydroxide. Solution was aided by stirring with a glass rod. The end point was determined by the disappearance of turbidity observed with flashlight through the deep blue solution. There was required 9.2 ml. of N/1 sodium hydroxide. In other runs, if it was suspected that too much sodium hydroxide had been added, a small amount of phthalein was precipitated by 5 per cent acetic acid and then more N/1 sodium hydroxide was added to just dissolve the precipitate. The solution was filtered by applying gentle suction. The final solution, 85.1 gm., was transferred to a sterilized amber bottle for delivery to the hospital.

The following radiation measurements were made on this batch at 9:30 A.M. November 21, 1947:

| | | *Per Cent* |
|---|---|---|
| *Radioactive iodine solution as received* | *0.60 r/8 hr. at 18 inches* | *of Total* |
| First liquor after extraction | 0.02 r/8 hr. at 18 inches | 3.6 |
| Washed carbon tetrachloride | 0.02 r/8 hr. at 18 inches | 3.6 |
| Mother liquor from T.I.P. | 0.09 r/8 hr. at 18 inches | 16.1 |
| Product | 0.43 r/8 hr. at 18 inches | 76.7 |
| Total | 0.56 r/8 hr. at 18 inches | |

This means that 76.7 per cent of the total radioactivity was obtained in the final product. The decrease in the total from 0.60 to 0.56 represents natural decay.

*Dosage and Radiation Measurement Determinations on Animals.* Radioactive tetraiodophenolphthalein was given both orally and intravenously to 6 dogs, and roentgenograms revealed excellent shadows of the gallbladders. The gallbladder area of these dogs produced a high intensity of gamma-ray activity, further indicating that radioactive tetraiodophenolphthalein was concentrated in the gallbladder similar to non-radioactive tetraiodophenolphthalein. Therefore, the liver and the extrahepatic biliary tract was directly irradiated by the beta and gamma rays resulting from the disintegration of the $I^{131}$ in the compound. This was also confirmed by monitoring the bile draining from a cholecystostomy and by liver tissue radioautographs.

The clinical and lethal doses of radioactive tetraiodophenolphthalein were found to be within the same ranges as established by Graham, Cole, Copher and Moore[1] for sodium tetraiodophenolphthalein. Results are listed in Table 1.

As a result of these observations 0.14–0.20 gm/kg. of radioactive tetraiodophenolphthalein was used as a dose to produce a satisfactory cholecystogram with the least reaction. Radioautographs of liver tissue revealed that the radioactive material was concentrated in the biliary system, and microscopic study of the various organs of these animals did not demonstrate evidence of severe tissue damage. However, in the region of the gallbladder bed, there were questionable areas of cell destruction. Several animals have survived more than two years after they were given the first of many doses of radioactive tetraiodophenolphthalein.

In estimating the total equivalent roentgens due to $I^{131}$ disintegrations which reached and penetrated to significant depths in the wall of the biliary system, the following calculations and conditions were used:

Thickness of gallbladder wall was measured as 2 mm.

Density of bile and gallbladder tissue was 1 (identical with density of water).

Maximum range of beta particles of $I^{131}$ in water was 2.2 mm.

Average range of beta particles of $I^{131}$ in water was 0.5–0.7 mm.[2]

Total volume of gallbladder was 12.2 cc. (assuming spherical shape).

In calculating the radiation flux through the gallbladder mucosa, a distance equal to the average range of the beta particles, 0.5 mm. was assumed to be the effective distance of the irradiation source in the layer of bile immediately adjacent to the gallbladder mucous membrane. Thus the gallbladder mucosa effectively received beta-ray irradiation only from the radioactive bile (irradiation shell volume, see Legend 1 of Fig. 1) lying within 0.5 mm. of the mucosal surface. Also roughly, only 50 per cent of the beta rays from this radioactive region could reach the mucosal surface, the remainder being emitted in the opposite direction. On the other hand, the total gamma irradiation arose from the entire volume of radioactive bile in the gallbladder.

All calculations given are rounded off to the nearest significant figure. These calculations are very approximate and intended only to indicate magnitude of dosage.

To determine the amount of radiation that the biliary system received during the half-life of $I^{131}$, bile specimens from each animal were assayed daily. To obtain such daily specimens of radioactive bile, cholecystotomies were performed and ten days after operation when the wound had healed and the animals appeared normal in all respects, they were given radioactive tetraiodophenolphthalein and bile specimens were collected from the gallbladder through indwelling tubes.

The method we used in arriving at the amount of radiation received by the gallbladder wall is given in detail by the following instance. The results on other animals were obtained in a similar manner. Dog No. 1—weighed 18.6 kg. The gallbladder had a volume of 12.2 cc. At 3:00 P.M. on July 3, 1948, this animal was given 21.1 millicuries of radioactive tetraiodophenolphthalein injected intravenously. Assuming no excretion, at 3:00 P.M. July 10, 1948, 54 per cent (7 days, 46 per cent decay) should remain. Forty-six per cent of 21.1 mc. is

TABLE I

AMOUNTS OF RADIOACTIVE TETRAIODOPHENOLPHTHALEIN GIVEN TO DETERMINE THE SAFE CLINICAL DOSAGE LIMITS

| Animal | Method of Administration | Amount of Radioactive Iodine, gm/kg. | Reactions | Cholecystogram |
|---|---|---|---|---|
| Dog. No. 1 | Orally | 0.13 | None | Normal visualization |
| Dog. No. 2 | Orally | 0.21 | Vomited | Not visualized |
| Dog. No. 3 | Intravenously | 0.17 | None | Normal visualization |
| Dog. No. 4 | Intravenously | 0.29 | Died in 12 hours | Not visualized |
| Dog. No. 5 | Intravenously | 0.12 | None | Normal visualization |
| Dog. No. 6 | Intravenously | 0.10 | None | Normal visualization |
| Dog. No. 7 | Intravenously | 0.18 | None | Normal visualization |
| Dog. No. 8 | Intravenously | 0.39 | Died in 18 hours | Normal visualization |
| Dog. No. 9 | Intravenously | 0.35 | Died in 24 hours | Normal visualization |
| Dog. No. 10 | Orally | 0.11 | None | Normal visualization |
| Dog. No. 11 | Intravenously | 0.10 | None | Normal visualization |
| Dog. No. 12 | Intravenously | 0.24 | None | Normal visualization |
| Dog. No. 13 | Intravenously | 0.13 | Death from faulty anesthesia | Not visualized |

Average of 0.34 gm/kg. =lethal dose.
Average of 0.14 gm/kg. =clinical dose.

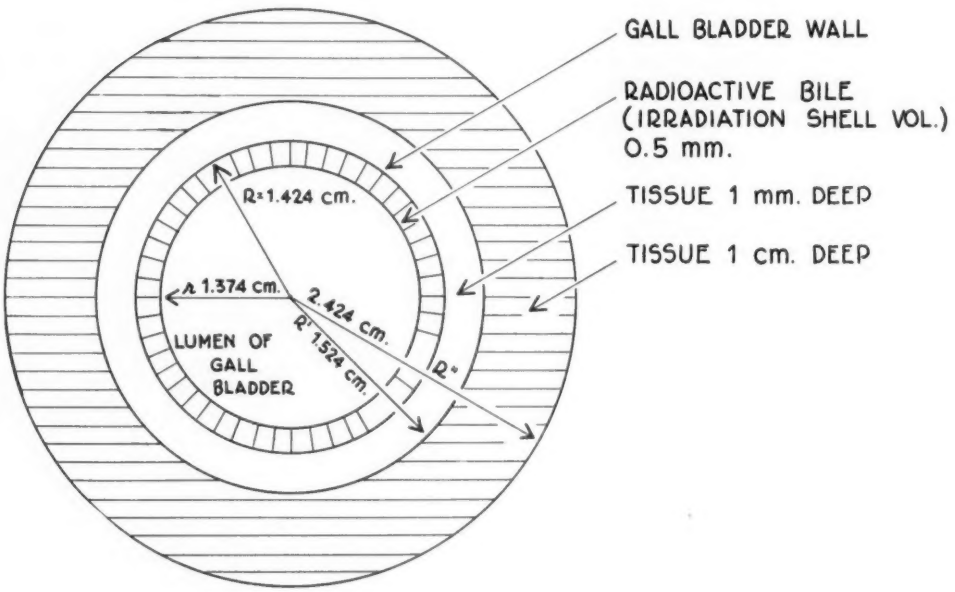


FIG. 1. Cross section of gallbladder and surrounding tissue with calculations for determining rep/cc. of radioactive bile.

1. Calculation of volume of the effective radioactive bile.
   Formula for volume of sphere is $4.189R^3$
   Known volume of gallbladder is 12.2 cc.
   $\therefore \quad 4.189R^3 = 12.2$ cc.
   $R = \sqrt[3]{12.2/4.189} = 1.424$ cm. (inside radius of gallbladder)
   1.424 cm. $-$ 0.05 cm. $=$ 1.374 cm. $= r$
   $4.189\ (1.374)^3 = 10.85$ cc.
   12.2 cc. $-$ 10.85 cc. $=$ 1.35 cc. $=$ volume of radioactive bile lying within 0.05 cm. of mucosa and is the source of beta radiation. This will be referred to as "irradiation shell volume."
2. Calculation of the volume of tissue in which the beta and gamma radiation was dissipated.
   $R' = R + 0.1$ cm. (use 0.1 cm. to arrive at maximal estimate of volume involved)
   $R' = 1.424$ cm. $+ 0.1$ cm. $= 1.524$
   $\therefore \quad 4.189\ (1.524)^3 = 14.82$ cc.
   14.82 cc. $-$ 12.2 cc. $=$ 2.62 cc. $=$ volume of tissue radius of 1 mm. from inner surface of gallbladder and parallel to its surface (maximal estimate)
3. Calculation of equivalent roentgens from interaction of beta rays from irradiation shell volume with 2.62 cc. of tissue.
   1 roentgen delivers 83 ergs of energy to 1 gm. of tissue or 1 cc. of bile
   1 $\mu$c. yields $3.7 \times 10^4$ particles/sec.
   1 $\mu$c. yields $3.2 \times 10^9$ particles/24 hours
   $K = 1.6 \times 10^{-6}$ (conversion factor for mev. to ergs)
   Average energy of beta particles of $I^{131} = 0.205$ mev.

$$\text{rep/cc.} = \frac{(\text{Particles in 1 } \mu\text{c.})\ (\text{Av.E})\ (K)\ (\mu\text{c. in 1 cc. or gm.})}{\text{No. ergs/rep.}} \quad (\times \tfrac{1}{2} \text{ for geometrical factor})$$

9.7 mc. Therefore 21.1 $-$ 9.7 $=$ 11.4 mc. was theoretical residue in tissue, assuming no excretion. Actually at 3:00 P.M. July 10, 1948, the liver contained 942 microcuries and the gallbladder contained 0.12 $\mu$c. Total daily radioactivities in bile are shown in Table II.

Daily rep (roentgens equivalent physical) values for the gallbladder wall due to beta radiation as calculated on the basis of the experimentally determined quantities of radioactivity in the effective irradiation shell volume (Column 4, Table II) are shown in Table III.

TABLE II

SPECIFIC ACTIVITY OF RADIOACTIVE BILE SPECIMENS FROM CHOLECYSTOTOMY

| Date | Amount of Bile | Radioactivity in 1 cc. of Specimen | Radioactivity in Irradiation Shell Volume (1.35 cc.) | Radioactivity of All Bile in Gallbladder Due to Beta Particles |
|---|---|---|---|---|
| July 4 | 2 cc. | 14.50 μc. | 19.5 μc. | 176.00 μc. |
| July 5 | 1 cc. | 8.20 μc. | 11.1 μc. | 101.00 μc. |
| July 6 | 2 cc. | 0.43 μc. | 0.65 μc. | 5.20 μc. |
| July 7 | 2 cc. | 0.09 μc. | 0.12 μc. | 1.10 μc. |
| July 8 | 3 cc. | 0.03 μc. | 0.04 μc. | 0.44 μc. |
| July 9 | 3 cc. | 0.02 μc. | 0.03 μc. | 0.28 μc. |
| July 10 | 3 cc. | 0.01 μc. | 0.01 μc. | 0.12 μc. |

The calculations involved are described in detail in the drawing in Figure 1 and in the legend beneath it together with the values used for substitution in Table III and the calculations worked out in the legend below it.

The gamma dosage delivered to the tissue from the radioactive irradiation volume was estimated as approximately 3–5 per cent of the beta dosage. To this it was required to add the dosage originating from the whole bile volume. Roughly, this component of dosage could be obtained merely by multiplying the 3–5 per cent of the beta rep value by the ratio of the total bile volume to the irradiation shell volume. The values so obtained are shown in Column 3, Table III. The tissue adjacent to the gallbladder extending in radius 1 cm. beyond the wall (see Fig. 1) received effectively only gamma radiation. This total gamma dosage for this tissue was no more than 5 rep for the total period (one week).

Similar dosage ranges were recorded with other animals studied. Hence it appears that the dose was well below the cancerocidal level.

Liver dosages in 3 different animals were calculated to be 75,000 total roentgens in nine hours, 137,000 roentgens in eighteen hours, and 420,000 roentgens in twenty-four hours on the seventh day. These liver exposures may be within cancerocidal ranges according to the volume dose conception of Mayneord and Clarkson,[3] especially if they could be repeated several times per week for several weeks to offset the rapid drop in radiation intensity in the first twenty-four hours.

Necropsy findings showed questionable growth and microscopic changes in the liver and gallbladder of all dogs at the dosage ranges which were proved to be clinically safe. Since these dosage ranges were at the lower therapeutic level, we felt justified in giving radioactive tetraiodophenolphthalein to humans. Also, when it is known that errors in determinations of dosage are great, frequently varying from two to five times the correct value, we felt that a clinical trial might reveal beneficial effects.

Patients with cancer of the liver were

TABLE III

DAILY DOSAGE IN BILE MUCOSA

| Date | Beta rep in Tissue 1 mm. Deep | Approximate Gamma Dosage, rep (gallbladder wall) |
|---|---|---|
| July 4 | 47.0 | 13.0 |
| July 5 | 27.0 | 7.3 |
| July 6 | 1.4 | 3.8 |
| July 7 | 0.3 | — |
| July 8 | 0.09 | — |
| July 9 | 0.06 | — |
| July 10 | 0.03 | — |

76+14=90 total rep/due to beta and gamma radiations delivered to gallbladder wall.

Liver assay on 7th day.

Liver weighed 680.0 gm.; specimen weight 13.1 gm. which contained 18.15 μc. on 7th day. Total liver contained 941.9 μc. or 1.38 μc/gm. liver on the 7th day.

$$\frac{(3.2\times10^{9})(.205)(1.6\times10^{-6})(1.38)}{83}=17.5 \text{ rep}$$

selected after exploratory laparotomy revealed the primary site in the biliary system or of an undeterminable primary site. Four patients were treated in this manner.

*Clinical Observations*

Case I. The first patient, a white female, aged seventy-seven (History No. 1-0-47-8867), was explored by laparotomy and found to have metastatic carcinoma of the liver with the primary site in the gallbladder. Following the laparotomy, there was a steadily retrogressive clinical course. This patient was given 34 mc. of radioactive tetraiodophenolphthalein intravenously on the sixth postoperative day. The patient died on her seventeenth postoperative day—nine days after a single injection of radioactive tetraiodophenolphthalein. Autopsy revealed primary adenocarcinoma of the gallbladder with metastatic extension to the liver, ribs, skull and vertebrae. There was no microscopic evidence of radiation effect in specimens obtained from the autopsy.

Specimens were obtained from various organs and completely ashed and then monitored for radioactivity. The results are given in Table IV. Assuming no excretion, 34 mc. of radioactive tetraiodophenolphthalein injected on November 21 would disintegrate to 11.5 mc. by December 4, the date of the autopsy. Actually 5 mc. remained and 6.5 mc. were excreted.

Case II. The second patient, white female, aged fifty-one (History No. 1-0-47-7421), was admitted September 9, 1947, with a firm mass in the right upper quadrant. The abdomen was explored September 29, 1947, and the gallbladder was found to be the center of a mass which consisted of the transverse colon, omentum, lower right lobe of the liver, and apparently the duodenum. There was marked inflammatory reaction around this mass, and above the mass on the surface of the right lobe of the liver there were several large button-like nodules, white in color, hard in consistency, which had the gross appearance of carcinoma. A biopsy of the liver nodule indicated a metastatic carcinoma. This patient was given 52 mc. of radioactive tetraiodophenolphthalein intravenously on October 23, 1947, without any reaction. No gallbladder shadow could be seen on film. Geiger-Müller counts were intense over the liver area and the palpable mass. On November 6, 1947, the patient was given a second injection of 22 mc. without reaction. Counts were intense over liver area but not in the gallbladder area.

The patient experienced a slight initial improvement following the operation and irradiation. She became gradually weaker, with marked anorexia, and later with nausea and vomiting. Patient died at home on forty-eighth postoperative day. Autopsy permission could not be obtained.

Case III. The third patient, white female, aged sixty-seven (History No. 1-0-47-772), had gallbladder attacks for forty years, consisting of sharp right upper quadrant pain, bloating, discomfort after fatty foods, attacks of chills, fever, jaundice. Physical examination revealed a large mass in the mid-abdomen. Exploratory laparotomy was performed October 1, 1947, and revealed the right and left lobes of the liver studded with metastases. Diagnosis at the time of operation was carcinoma of gallbladder or perhaps pancreas without cystic duct obstruc-

Table IV

$I^{131}$ distribution in postoperative cancer patient

| | μc/gm. of Tissue | Total Weight of Organs in gm. | Total Radioactivity Present in Organs in μc. | Radiation Dosage | |
|---|---|---|---|---|---|
| | | | | rep | Total Roentgens |
| Normal liver | 1.07 | 3,500 | 3,750 | 13.5 | 47,200 |
| Gallbladder wall | 2.41 | 20 | 48.2 | 30.4 | 610 |
| Carcinoma of gallbladder | 0.50 | ? | | 6.3 | ? |
| Thyroid | 1.47 | 7.5 | 11 | 18.6 | 140 |
| Bone marrow | 1.22 | 1,000 | 1,220 | 15.4 | 15,000 |
| Total | | | 5,025 μc. | | 63,000 r |

tion. This patient was given the following doses of radioactive tetraiodophenolphthalein:

| | |
|---|---|
| October 10, 1947 | 38 mc. |
| October 17, 1947 | 13 mc. |
| November 27, 1947 | 43 mc. |
| December 12, 1947 | 50 mc. |

At no time could a gallbladder shadow be demonstrated on the roentgenograms. This patient had severe nausea and some anorexia after each injection. Geiger-Müller counts were extremely intense over the right upper quadrant and of a lesser uniform intensity over the body, roughly proportional to the volume of blood below the tube. There was no discernible increase in intensity of counts over the thyroid gland, or elsewhere in the body.

This patient's clinical course following laparotomy was one of slight initial improvement for the first three weeks followed by a period of about four weeks, when the clinical picture was stable. During the latter period, the patient was able to sit up in a chair for brief periods of time and was eating well. The last four weeks were of a gradually retrogressive course. The patient died twelve weeks after operation.

The clinical course of this patient was followed carefully with blood counts, liver and kidney function tests. All results of the tests were similar to the results obtained before surgery and radioactive isotope administration.

Pathological report on autopsy findings was mucinous carcinoma of the cystic duct and neck of the gallbladder, metastatic carcinoma to the liver, cholelithiasis, hydrops of gallbladder and atrophy of thyroid gland. Autopsy specimens could not be assayed for radioactivity.

Case IV. The fourth patient, white female, aged sixty-five (History No. 151411), was seen on August 22, 1947, in Washington University Clinics complaining of a mass in the abdomen of eight months' duration and a 30 pound weight loss during that period. She had no particular gastrointestinal or urinary complaints. Past history revealed episodes of jaundice and right upper quadrant pain twenty-nine years previously, for which cholecystectomy and appendectomy were done in 1918. In 1932 she had oophorocystectomy for ovarian cysts. Physical examination was essentially negative except for a large nodular, slightly tender mass extending across the right upper quadrant and epigastrium and extending down to the level of the umbilicus.

Exploration of the abdomen on September 30, 1947, showed all organs were normal except for a firm plaque about 8 cm. in diameter of very firm hard tissue which resembled carcinoma of the under surface of the liver. On the greater surface of the liver under the diaphragm were additional nodules. Pathological report of the biopsy from the left lobe of the liver was: Metastatic adenocarcinoma of liver.

This patient was given radioactive tetraiodophenolphthalein intravenously on the following dates:

| | |
|---|---|
| October 30, 1947 | 45 mc. |
| December 4, 1947 | 50 mc. |
| January 16, 1948 | 63 mc. |
| January 29, 1948 | 40 mc. |
| February 13, 1948 | 60 mc. |
| March 9, 1948 | 20 mc. |
| March 7 to 12, 1948 | Roentgen therapy to cervical spine |
| April 11, 1948 | 30 mc. |
| May 7, 1948 | 30 mc. |

This patient always experienced much nausea after each injection, but otherwise showed no untoward effects. She seemed to be more active and felt greatly improved. In the early part of March she began to feel pain in the cervical spine, and a roentgenogram revealed destruction of the lowest cervical vertebrae. Because of the pain in the neck, roentgen therapy was given simultaneously with the radio-

TABLE V

BLOOD VOLUME DETERMINATION ON CASE IV

| Cell Residue Sample—Counts/Min. | Serum Sample—Counts/Min. |
|---|---|
| ooR = 5 | ooS = 184 |
| oR = 115,600 | oS = 188,000 |
| 1R = 354 | 1S = 286 |
| 2R = 358 | 2S = 264 |

Sample oo represents blood before any material was given; *i.e.*, represents radioactive iodeikon given three weeks before.
Sample o = blood injected (10 cc. given).
Sample 1 = taken 10 minutes after injection.
Sample 2 = taken 20 minutes after injection.

$$\text{Whole Blood Volume} = \frac{\text{Counts/min. in blood given}}{\text{Counts/min. in blood sample}}$$

times volume of blood given

$$\text{WBV} = \frac{\text{oR}}{\text{1R}} \times 10 = \frac{115{,}600}{354} \times 10 = 3270$$

$$\frac{\text{oR}}{\text{2R}} \times 10 = \frac{115{,}600}{358} \times 10 = 3230$$

$$= 3250 \text{ cc.}$$

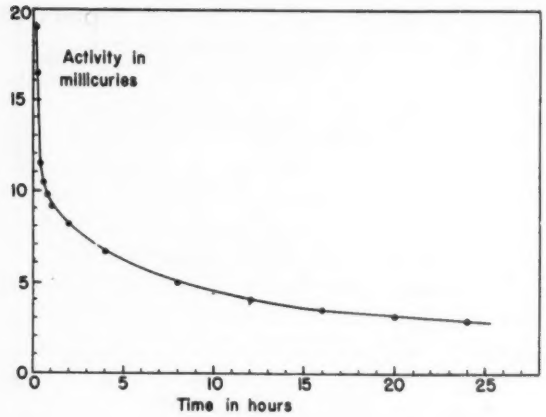


FIG. 2. Radioactivity of total circulating blood. Case IV.

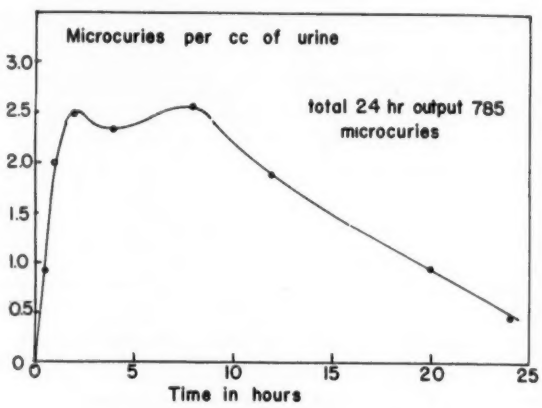


FIG. 3. Urinary excretion of radioactive iodeikon. Case IV.

active tetraiodophenolphthalein. Monitoring with the Geiger-Müller counter revealed no concentration of the isotope in metastatic lesions of the cervical spine. This patient seemed to respond favorably to isotope therapy, always feeling improved after an injection. She was

TABLE VI

ACTIVITY OF TOTAL CIRCULATING BLOOD IN MILLICURIES ON CASE IV

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|
| Blood Sample | Hematocrit | Reading on Electroscope in Seconds of 0.01 cc. of of Plasma | μc/1.0 cc. of Plasma[1] | μc. Contained in Plasma of 1.0 cc. of Whole Blood[2] | Reading on Electroscope in Seconds of 0.1 cc. Cell Residue | μc/cc. of Cell Residue[3] | μc. Contained in Cells of 1.0 cc. of Whole Blood[2] | Total Activity Whole Blood (μc/cc. Blood) | Activity[4] of Total Circulating Blood in Millicuries |
| 3 10 min. | 36.6 | 55.5 | 7.90 | 5.00 | 116 | 0.224 | 0.082 | 5.08 | 16.5 |
| 4 20 min. | 35.7 | 80.5 | 5.45 | 3.50 | 128 | 0.203 | 0.073 | 3.57 | 11.6 |
| 5 30 min. | 35.5 | 90 | 4.88 | 3.15 | 135 | 0.197 | 0.068 | 3.22 | 10.5 |
| 6 45 min. | 36.5 | 94 | 4.66 | 2.96 | 204 | 0.127 | 0.046 | 3.01 | 9.8 |
| 7 1 hr. | 35.4 | 102 | 4.30 | 2.78 | 210 | 0.124 | 0.044 | 2.82 | 9.2 |
| 8 2 hr. | 38.5 | 109.5 | 4.02 | 2.47 | 227 | 0.114 | 0.044 | 2.51 | 8.2 |
| 9 4 hr. | 40.0 | 133 | 3.33 | 2.00 | 295 | 0.088 | 0.035 | 2.03 | 6.7 |
| 10 8 hr. | 38.0 | 178 | 2.46 | 1.53 | 447 | 0.058 | 0.022 | 1.55 | 5.15 |
| 11 12 hr. | 33.8 | 233 | 1.88 | 1.24 | 684 | 0.038 | 0.013 | 1.25 | 4.15 |
| 12 16 hr. | 37.7 | 257 | 1.70 | 1.06 | 633 | 0.041 | 0.015 | 1.08 | 3.5 |
| 13 20 hr. | 36.0 | 290 | 1.51 | 0.97 | 905 | 0.029 | 0.010 | 0.98 | 3.2 |
| 14 24 hr. | 34.8 | 390 | 1.15 | 0.75 | 1,095 | 0.024 | 0.008 | 0.76 | 2.5 |

[1] Determined by comparison with uranium standard at same geometry; 0.313 μc. of standard gave 50 unit scale deflection in 140 seconds on 3rd shelf therefore formula $\frac{.313 \times 140}{\times \text{sec.}} = \mu\text{c. of unknown sample.}$

[2] Corrected by hematocrit readings.

[3] Determined by comparison with uranium standard at same geometry; 0.313 μc. of standard gave 50 unit scale deflection in 83 sec. at 2nd shelf therefore formula $\frac{.313 \times 83}{\times \text{sec.}} = \mu\text{c. of unknown sample.}$

[4] Figures based on determination of circulating blood volume at beginning of experiment of 3,250 cc.

studied in detail as to the fate of the isotope in blood and urine.

The patient's blood volume was determined by the method devised by R. T. Niest and W. J. Trautman, Jr. (see Table v). The total blood volume was 3,250 cc. She was given 20 mc. of radioactive tetraiodophenolphthalein intravenously, and simultaneous blood and urine specimens were taken as indicated in Tables VI and VII and illustrated in Figures 2 and 3. These studies show that the dye is absorbed rapidly from the blood stream—50 per cent in thirty minutes, 66 per cent in four hours, 75 per cent in eight hours, and 87 per cent in twenty-four hours.

Only 3.9 per cent of the total millicuries injected was excreted in urine in the first twenty-four hours. This patient had no bowel movements during the period of observation. However, observation in dogs showed that large amounts of unabsorbed dye are excreted in the feces.

This patient was discharged from the hospital and is living. It has been difficult to make further studies on this patient. However, examination reveals that her right upper quadrant abdominal mass has not changed in size. The metastatic focus in the cervical vertebrae has not responded to either isotope therapy or roentgen therapy. Monitoring with the Geiger-Müller counter reveals no concentration of isotopes in the metastases.

TABLE VII

URINARY EXCRETION OF RADIOACTIVE IODEIKON IN CASE IV

20 mc. injected

| Specimen | Volume in cc. | μc/cc. | Total μc/specimen |
|---|---|---|---|
| 1– ½ hr. | 55 | 0.93 | 51.5 |
| 2– 1 hr. | 23 | 2.00 | 45.8 |
| 3– 2 hr. | 53 | 2.50 | 135.2 |
| 4– 4 hr. | 54 | 2.35 | 127.0 |
| 5– 8 hr. | 67 | 2.57 | 172.5 |
| 6–12 hr. | 54 | 1.86 | 100.5 |
| 7– | | | |
| 8–20 hr. | 124 | 0.96 | 113.3 |
| 9–24 hr. | 90 | 0.44 | 39.4 |
| Total 24 hour output | | | 785.2 microcuries |

## SUMMARY AND CONCLUSIONS

The findings from dogs and from the human reveal that:

(1) Radioactive tetraiodophenolphthalein is metabolized and excreted in the same manner as the non-radioactive compound.

(2) The radiation resulting from the disintegration of artificially radioactive tetraiodophenolphthalein is dissipated primarily within the biliary system and adjacent liver tissue.

(3) From calculations of tissue dosage it would seem probable that radioactive tetraiodophenolphthalein does not produce radiations in sufficient quantity (maximum of the order several hundred rep in one week) to be therapeutically effective in malignancy of the gallbladder, but may possibly be effective in the liver.

(4) It should be possible to treat selectively with radiation by combining radioactive isotopes with elements or compounds that have special affinities for certain organs or body systems. This technique is in effect similar to a "guided missile" and holds promise for treatment of other parts of the body.

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# THE EFFECT OF TOTAL BODY ROENTGEN IRRADIATION ON THE LONG BONES OF HAMSTERS

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THE effect of ionizing radiations on the growth of bone in animals has been the subject of many investigations. Most of the studies in which the histologic changes have been described involved experiments in which the bone was directly irradiated.[1,5,7,10] There have been few reports, however, of the histologic changes in bone following total body irradiation. Heller[6] and Bloom[3] described the changes in the long bones of rats, mice, guinea pigs and chicks following roentgen irradiation at the $LD_{50}$ level.

No studies have been made of the bone of hamsters subjected to as much as 1,500 r total body irradiation, which kills the animals within ten days, or to so much radiation that death occurred under the roentgen-ray beam (approximately 110,000 r in $3\frac{1}{4}$ hours). The purpose of this paper is to report the results of a histologic study of the long bones of hamsters so treated. These studies relate to changes in three hours or four days following initiation of irradiation.

## MATERIALS AND METHODS

Healthy hamsters, inbred in our laboratory (original stock derived from Northfield Hamstery), were used. They were divided into two groups. One, comprising young male and female animals of about six weeks of age and older male and female animals of about nine months of age, was exposed to 1,500 r roentgen radiation. A second similar group was irradiated continuously until all were moribund. The tissues were removed before respiration and circulation ceased. This stage usually occurred after approximately three hours of continuous radiation at 184 kv. (peak), 30 ma., with opposing tubes and no external filters. The dose rate was 510 r/min. at 35.5 cm. in air for a total of about 110,000 r. For the young hamsters, death under the beam resulted at about 80,000 r, or after approximately two hours and forty minutes.

At death, the hind legs of all animals were removed immediately, trimmed of skin and most of the muscle, and fixed whole in Bouin's solution. Decalcified paraffin sections were stained with hematoxylin and eosin, Masson's trichrome, toluidine blue, bismark brown and Laidlow's silver stain.

Because of the known radiation sensitivity of the epiphyseal plate and the shaft of the tibia these areas were used for description and illustration.

## EXPERIMENTAL DATA

### *$LD_{100}$/10 Days, 1,500 r Single Dose*

*Control.* The normal epiphyseal cartilage consists of a row of fourteen to sixteen columnar cells and four to six hypertrophic cartilage cells. The zone of erosion, located immediately below the degenerating hypertrophic cartilage cells, is well vascularized by capillaries which are dilated and filled with red blood cells. The bony spicules of the primary spongiosa are lined by osteoblasts. There is an occasional multinucleated osteoclast on a bony spicule of the primary spongiosa as well as in the layer of degenerating cartilage cells (Fig. 1*A*).

With the Masson trichrome stain, the cytoplasm of the columnar cartilage cells stains pink. The epiphyseal plate is densely metachromatic with toluidine blue, and there are numerous metachromatic fibers in the undifferentiated mesenchyme of the metaphyses.

The marrow cavity is filled with hematopoietic tissue (Fig. 2*A*), consisting of all the different stages of developing erythrocytes and granulocytes.

*Irradiated to 1,500 r.* Tissues were taken at three hours and just before the expected death at about three or four days. Three hours following irradiation, the vascular channels are dilated and engorged with red blood cor-

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puscles. There are focal areas of hemorrhage, and some slight edema in the marrow space. There is an occasional pyknotic nucleus in the leukopoietic marrow. Three or four days following irradiation the marrow of the metaphysis is replaced by a loose fibrous connective tissue. This tissue is mucoid in appearance with hematoxylin and eosin stain, but mucihematin stains for connective tissue mucin are negative. Many of the nuclei of this tissue are spindle shaped and are abnormally large. Large multinucleated osteoclasts are present in the zone of erosion and on the metaphyseal bony spicules. The nuclei in many of the hypertrophic cartilage cells are swollen and edematous. There are very few osteoblasts lining the spicules of cartilage and primary spongiosa (Fig. 1*C*). Those which are present are abnormal in shape, assuming a long, thin, spindle shape instead of the usual polygonal one. The osteocytes are, for the most part, normal in appearance, although occasionally there are empty lacunae or a lacuna which is filled with a finely granular basophilic debris. There are innumerable fine proliferating capillaries (Fig. 2*B*) in the hemorrhagic marrow cavity and a large amount of edema. Few cells of the leukopoietic series are present. With Masson's trichrome stain, the collagenous nature of the fibroblastic proliferation in the metaphysis is identified.

Using Laidlow's silver staining technique for reticulum, one finds a tremendous overgrowth of reticulum in the marrow cavity, especially in areas closely associated with bone spicules (Fig. 1*F*). This consists of a meshwork of fine argyrophilic fibers which, in some areas, appears to originate from the "periosteum" surrounding the bone spicules of the primary and secondary spongiosa, and in other areas appears to originate from the dilated capillaries. The great edematous reaction in the marrow space is also demonstrated by use of this technique.

### *Older, Mature Animals*

*Control.* The epiphyseal cartilage plate contains three or four hypertrophic cells and five or six columnar cells per row. These columns are separated by more basophilic matrix than is found in the younger animals. There is, in most animals, subepiphyseal bony linkage. The bony spicules of the primary spongiosa are lined by osteoblasts, although they are not as numerous as in the younger animals. Occasionally the marrow contacts the cartilage. Here the zone of erosion is still well vascularized. The marrow contains much more fat than is present in younger animals, but it is otherwise essentially the same (Fig. 2*C*). The cytoplasm of the columnar cells in the cartilage row stains bright red with Masson's trichrome stain. The epiphyseal cartilage, as well as many fibers in the marrow of the zone of erosion and metaphysis, shows metachromatic staining with toluidine blue.

*Irradiated to 1,500 r.* Three hours following irradiation there are changes which are identical with those described for the younger animals. Four days after irradiation to 1,500 r and just before death, the epiphyseal cartilage is apparently normal, both in the number of cartilage cells per column and in the degree of ossification of the cartilage plate. The cytoplasm of the columnar cells does not stain red with Masson's stain. The metaphyseal marrow is replaced by a loose fibrous connective tissue, some of which shows fibrinoid degeneration. There is hemorrhage in this area, with many well preserved as well as many degenerating red blood cells. There is a great reduction in the number of osteoblasts which normally line the bony trabeculae of the metaphysis. Those which are present are plumper than normal or are spindle cells.

There is a marked decrease in the number of white blood cells and leukopoietic tissue, although there is some regeneration, especially in areas adjacent to the metaphyseal spicules of bone. The normal marrow is almost completely replaced by red blood cells and degenerating red blood cells. It is well vascularized. Throughout the marrow cavity there is a finely granular acidophilic precipitate. With Masson's stain, there is a finely granular basophilic mucoid-like mass of material which occupies the areas between the dense collections of red blood cells (Fig. 2*D*). In many areas, this gelatinous material surrounds small blood vessels. Occasional spindle cells are seen closely associated with this mucoid material. In some areas, the spindle cells appear to be proliferating vascular endothelial cells.

There is an increase in fibrous connective tissue around the bony spicules of the secondary spongiosa. There are many dilated and engorged vascular sinuses in this area and throughout the marrow cavity. The myelocytes have a granular cytoplasm with abnormal nuclei.

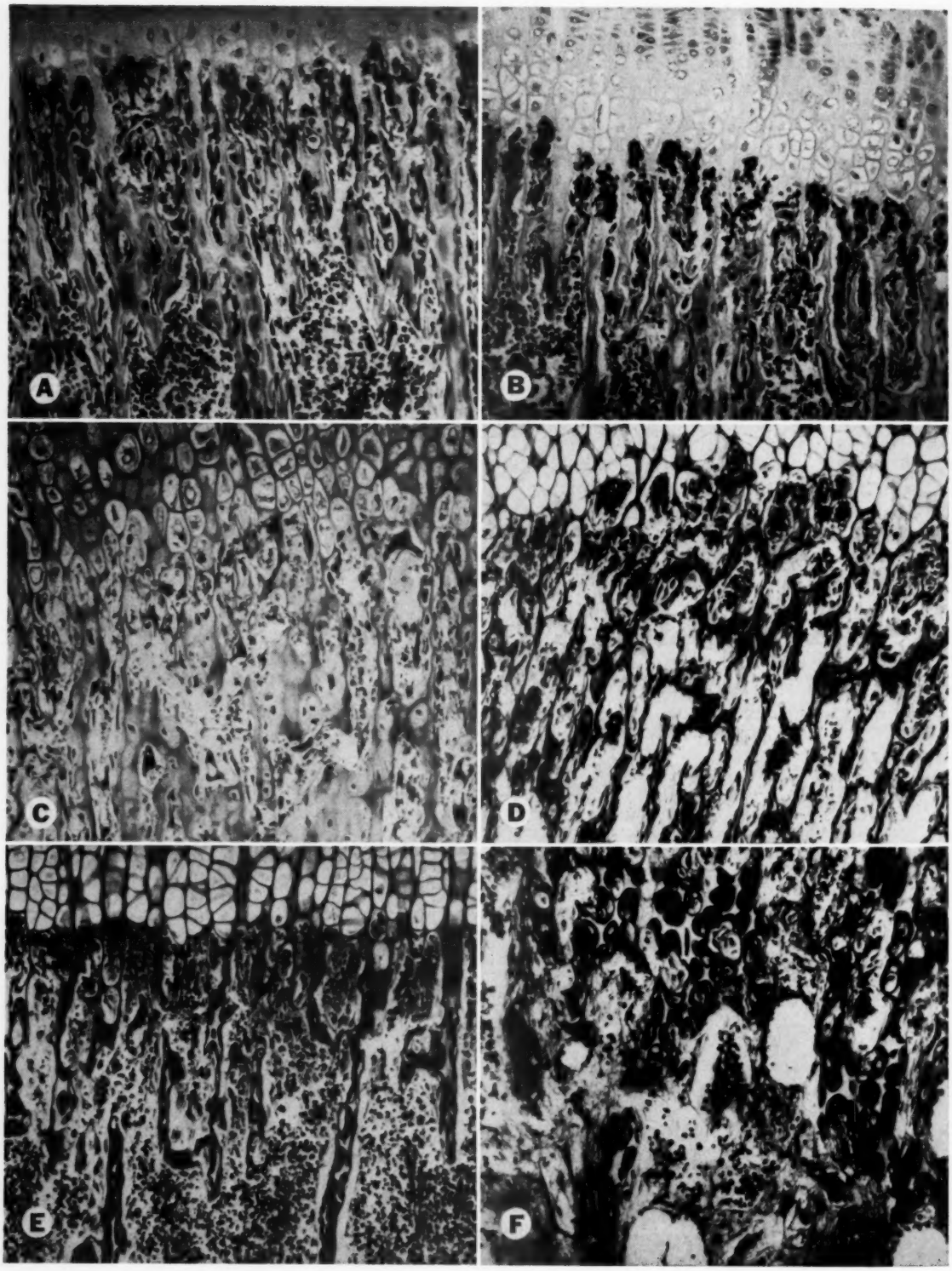


FIG. 1. Photomicrographs of the metaphyses of the tibia.

(*A*) Normal young animal. The zone of erosion is well vascularized. The spicules of the primary spongiosa are lined by osteoblasts. (Hematoxylin and eosin stain.)

(*B*) Young animal, irradiated to near death under roentgen-ray beam (110,000 r in $3\frac{1}{4}$ hours). The

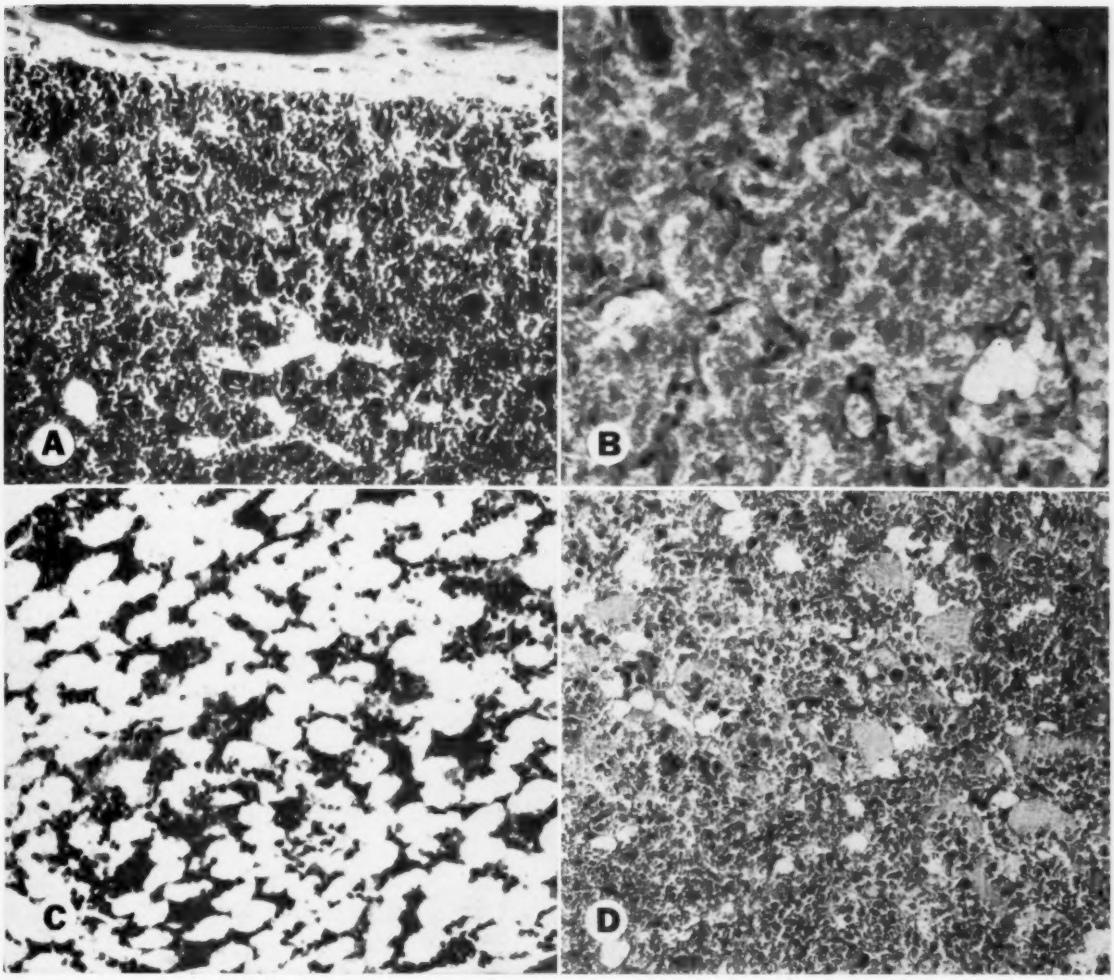


Fig. 2. Photomicrographs of bone marrow of shaft.

(*A*) Normal bone marrow, young animal. (Hematoxylin and eosin stain.)

(*B*) Young animal, four days following 1,500 r total body irradiation. The marrow is hemorrhagic and almost completely devoid of leukopoietic cells. There is an increase in vascularity.

(*C*) Normal bone marrow, old animal. (Masson's trichrome stain.)

(*D*) Old animal, four days following 1,500 r total body irradiation. The marrow is hemorrhagic. There are occasional abnormally shaped cells of the granulocytic series. Masses of mucoid material are clearly illustrated. (Trichrome stain.)

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osteoblasts have almost completely disappeared from the bony spicules of the primary spongiosa. (Hematoxylin and eosin.)

(*C*) Young animal, four days following 1,500 r total body irradiation. The marrow is replaced by fibrous connective tissue. An occasional abnormally formed osteoblast is present. Large multinucleated giant cells are located at the zone of erosion and in the metaphysis. (Hematoxylin and eosin.)

(*D*) Normal young animal, Laidlow's silver stain. A small amount of reticulum is seen in the zone of erosion.

(*E*) Young animal, irradiated to near death under the beam (110,000 r in $3\frac{1}{4}$ hours). There is a finely granular precipitate in the zone of erosion, and a slight increase in reticulum. (Laidlow's silver stain).

(*F*) Young animal, four days following 1,500 r total body irradiation. There is a tremendous increase in reticulum. Spindle cells are also seen. (Laidlow's silver stain.)

*Death under the Beam, $LD_{100}/3$ Hours, 110,000 r*

*Young Animals*

In the younger animals irradiated to death under the beam, the hypertrophic cells of the epiphyseal cartilage in some areas show swelling and edema, while in other areas they have a small pyknotic nucleus. The zone of erosion is hemorrhagic.

An occasional subepiphyseal or metaphyseal bony spicule is fractured. There is a reduction in the number of osteoblasts lining the bony spicules of the metaphysis (Fig. 1*B*). The marrow is hemorrhagic and edematous, and one finds numerous degenerating white blood cells with pyknotic nuclei. Staining with Laidlow's silver technique demonstrates the edema in the marrow spaces, as well as a slight increase in reticulum (Fig. 1*E*). There is a decrease in the metachromasia of the subepiphyseal areas.

*Older, Mature Animals*

In the older animals killed under the beam the epiphyseal cartilage is almost normal. One sees an occasional swollen hypertrophic cartilage cell. In the zone of erosion there are many extravascular red blood cells and a finely granular acidophilic debris. There is a decrease in the number of osteoblasts around the metaphyseal bony spicules. Many of the osteoblasts which remain are swollen and have a finely granular cytoplasm. The bone marrow is hemorrhagic, and there are many degenerating white blood cells with pyknotic nuclei. The blood sinuses are dilated and filled with red blood cells. Use of toluidine blue stain demonstrates a decrease in metachromatic material in the zone of erosion and metaphyseal marrow. In these older animals Laidlow's silver stain shows no increase in reticulum.

## DISCUSSION

Previous workers, who used $LD_{50}/30$ days on rats, mice, rabbits, guinea pigs, and chicks described histopathological changes similar to those which we found with hamsters at 1,500 r. In addition, we describe histopathological changes following death under the beam, the most significant of which are hemorrhage and destruction of osteoblasts. The findings of destruction of the hematopoietic cells of the marrow with replacement by gelatinous material, fibrosis of the marrow and the presence of spindle cells, all of which were reported by Heller[6] and Bloom,[3] were confirmed by our study. Heller and Bloom describe the early changes at $LD_{50}/30$ doses as abnormal swelling of the cartilage cells and separation of cartilage and spongy bone through abnormal interdigitation between cartilage and metaphyseal spongy bone. The abnormal swelling of the cartilage cells was an occasional and minor finding in our study, nor did we find a separation of cartilage and spongy bone in our animals.

The disappearance of metachromatic fibers in the zone of erosion following roentgen irradiation has not been previously reported. This finding is particularly interesting in view of the recent reports by Patt *et al.*[8,9] who found that cysteine greatly reduces the sensitivity of rats and mice to lethal doses of total body roentgen irradiation, provided the amino acid is given before exposure. Cystine, methionine and sodium sulfide do not afford protection. The findings of Barron *et al.*[2] that radiation inhibits several of the enzymes, particularly the sulfhydryl-containing ones, is also related to this problem, since metachromasia is probably a property of the sulfate-containing mucopolysaccharides. In our study, while only the water stable fraction containing sulfhydryl groups would be preserved, the immediate disappearance of the metachromatic staining material following roentgen irradiation would seem to support the previous contentions that roentgen irradiation may cause death through interference with enzyme production or action, especially those enzymes containing sulfhydryl groups. Further studies of these phenomena are necessary to clarify the problem.

While increase in reticulum in the bones of irradiated animals has not been previously described, its presence in increased amounts was not unexpected. Maximow emphasized the relationship of these fibers to collagenic fibers, and many believe they

are "precollagenic." Corner[4] and others think that the reticular fibers are formed by vascular endothelium. In our animals, there is not only a tremendous fibrosis of the marrow, but also a proliferation of vascular endothelium. Reticulum would thus be expected to become more obvious in the marrow of irradiated animals than in the marrow of normal animals.

The most consistent finding in all the animals in this study was a hemorrhagic bone marrow. This finding has not been stressed previously for bone marrow although hemorrhage is a frequent finding in soft tissues. The changes are more severe in the younger hamsters than in the older ones. Otherwise, the findings for the two groups are identical.

SUMMARY

The long bones of animals irradiated to death under the roentgen-ray beam show a reduction in the number of osteoblasts lining the primary spongiosa; hemorrhage and edema of the marrow; a loss of metachromatic staining of the fibers in the zone of erosion; and degenerating hematopoietic cells.

Animals irradiated to 1,500 r and killed three hours later show vasodilatation, hemorrhage and edema of the marrow. This is accentuated in animals surviving three to four days. They show a fibrosis of the marrow, with spindle cells and vascular endothelial cells replacing a hemorrhagic and degenerating bone marrow. This develops some time after the first three hours following irradiation. There is a loss of osteoblasts lining the bony spicules of the primary and secondary spongiosa, a loss of metachromasia of the fibers in the zone of erosion, and a massive network of reticulum in the marrow cavity. These results are attributable to the ionizing radiations used.

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# CALCULATIONS FOR DISTRIBUTED SOURCES OF BETA RADIATION*†

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IN BIOLOGICAL or medical applications of beta-ray emitters it often happens that the radioactive isotope is deposited in tissue or in equivalent media in more or less discrete regions which have dimensions comparable to the range of the beta rays. This occurs usually as a result of either physiological concentration, of which iodine in the thyroid is the outstanding example, or as a result of mechanical concentration as in the case of small plastic beta-ray applicators. Other examples are suspension of organisms containing the activity in an inactive solution, and the inverse problem: the suspension of biological material in radioactive solutions. Experimental determination of the dose received under some of these conditions is a difficult problem at best, and in fact there are at present hardly any established techniques for such investigations. For this reason, theoretical dosimetry may be useful even if it is only approximate.

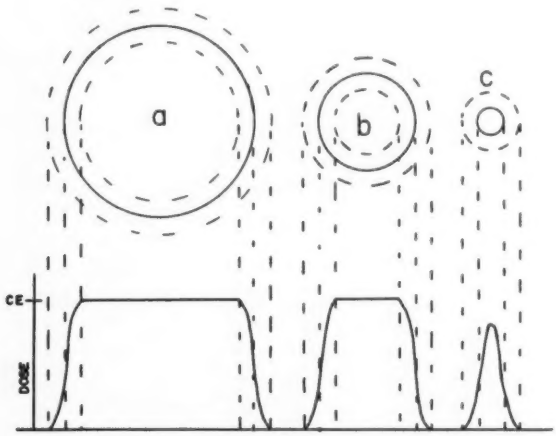


FIG. 1. Idealized representation of dose in distributed sources having various sizes relative to the maximum beta range. The maximum range is represented by the distance between the solid and dotted circles.

If the isotope is uniformly distributed in a large mass of homogeneous tissue, there will be a volume in which "irradiation equilibrium" exists. In this region the energy absorbed per gram of tissue is the same throughout. In the case of beta-ray emitting isotopes this region is enclosed within a shell of the tissue mass of thickness equal to the range of the most penetrating rays in the tissue (Fig. 1*a*). In this region the energy emitted is equal to the energy absorbed. Thus the dose is equal to $C$, the number of particles emitted per unit volume, times $E$, the average energy per particle. A paper by Marinelli, Quimby and Hine[3] is largely concerned with dosimetry in regions of irradiation equilibrium, and general considerations as well as specific data are noted there.

While theoretical dosimetry is simple under conditions of irradiation equilibrium, the problem becomes more difficult if the volume containing the beta-ray emitter has dimensions comparable with the beta range. In this case the dose throughout most of the structure will be less than $C$ times $E$ (Fig. 1*b*) and will in fact never reach this value in objects having diameters which are less than twice the beta range (Fig. 1*c*). Except for a few planes or points in certain shapes the dose can be computed only with a knowledge of the manner in which beta radiation is absorbed when passing through tissue. If dose as a function of distance from a point source is known, the dose inside and outside of extended objects may be obtained—at least in principle—by integration of the

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dose due to infinitesimal constituents.

As used in such a computation, the mathematical formulation of absorption should fulfill three requirements: first, it should, of course, be a good approximation to the physical process taking place; second, it should be valid for a large range of beta emitters; and third, it should be sufficiently simple to make the integration feasible without undue difficulties. None of these requirements can be fulfilled entirely, and they are to some extent mutually exclusive. At present, available information on the variation of dose with distance from a point source is incomplete—except for the case of $P^{32}$, which has been investigated by Loevinger,[2] but it seems clear that absorption functions of different beta emitters cannot be related by simple factors. It is also impossible to make a reasonable approximation which does not lead to fairly complex mathematical operations.

We have performed dosimetric computations for two classes of simple geometric shapes (slabs and spheres) using the approximation that beta radiation is absorbed exponentially. The complete mathematical derivations together with some detailed practical examples have been published elsewhere.[4] The purpose here is to restate the results of these computations in a form in which they may be more readily utilized by radiologists or radiobiologists and to discuss the degree of approximation which may be advantageously attained in practice.

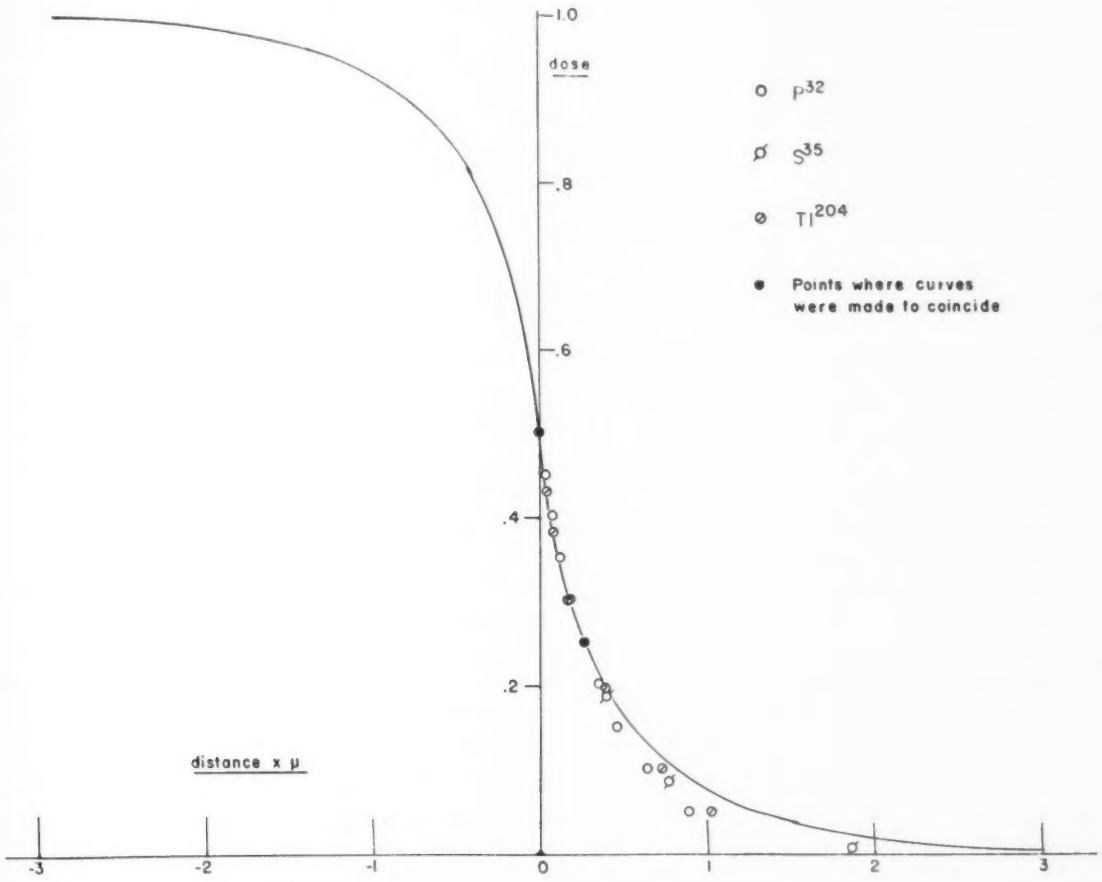


Fig. 2. Dose near the flat surface of a "thick" and extended plane source. The experimental points are from unpublished work by N. A. Baily.

Before discussing the question of approximation in detail, it may be well to point out that in computations of this sort precision is often rather pointless. While work in the physics laboratory can be done on exact geometrical shapes and doses can be measured with accuracy, biological structures are often none too well defined and radiobiological effects may be assayed only approximately. Thus, if one compares the chick thyroid with a small sphere which is uniformly permeated with $I^{131}$ at a concentration $C$, it must be realized that the thyroid is not exactly a sphere, that the activity is not uniformly distributed throughout, and that the determination of $C$ is attended by many sources of error. While it is quite true that one does not wish to add too much to this series of uncertainties, there is also no point in insisting on a theoretical dosimetry which is in error by less than about 10 per cent, especially since the biological effects of a 30 per cent variation in the actual dose are not likely to be distinguished with certainty. The approximation under discussion will be sufficient for any such instances in which neither the conditions nor the results of the experiment can be adequately quantified. It will be only in work involving definite numerical parameters (such as radiation chemistry, for instance) that experimental conditions warrant specific information on the degree of approximation obtainable.

Figure 2 shows the theoretical dose near the flat surface of a thick and extended concentration of a beta emitting isotope in an infinite mass of tissue. It may easily be shown from reasons of symmetry that the dose at the surface must be $CE/2$ and that the curve must approach the dose $CE$ in the interior of the volume containing the activity in the same manner as it approaches zero on the outside. The exact shape of the curve, of course, depends on the assumed absorption function. It might be pointed out, however, that a geometrical factor (the inverse square law) enters into the computation as well, and as a result the shape of the curve is not too sensitive to the type of absorption function chosen.

We are fortunate to have in this particular case some experimental data available, which are given in Figure 2. These values are from unpublished work performed by Baily.[1] It will be seen that the approximation for different isotopes is not the same, but that in all cases the computed dose is too high at great distances from the surface. Similarly, the dose inside the structure is underestimated. The absolute error is always less than about 5 per cent of $CE$, but the relative error becomes appreciable in regions where the dose is low. Since this curve is characteristic of a thick, flat beta-ray applicator, adaptation of the curve for such a source will lead to an overestimate of penetration.

In the process of fitting the theoretical curve to the experimental points, one can obtain an effective "average" absorption coefficient, $\mu$. A plot of log $\mu$ versus log $E_{max}$ ($E_{max}$ being the maximum energy of the beta rays emitted) appears linear for the three isotopes investigated by Baily. It would seem reasonable to employ this graph for isotopes having maximum beta-ray energies between the two extreme points in Figure 3. In this graph $\mu$ is given in reciprocal centimeters for materials of unit density (such as water, soft tissue and light plastic). When these data are used for materials of somewhat higher density they may be expected to be valid if the scale for $\mu$ is taken to express $cm^2/g$. It should be pointed out, however, that in cases where materials of different density are employed in the same arrangement scattering will introduce errors.

The assumption of exponential absorption implies that dose curves for different isotopes will be identical if the geometrical distances involved are expressed in terms of $1/\mu$. This follows from the simple fact that, if in the expression $e^{-\mu A}$, $A$ is replaced by $a=\mu A$ the resulting expression $e^{-a}$ becomes invariant with respect to $\mu$. If curves expressing $e^{-a}$ or some function thereof are plotted as a function of $a$, the value of the

graph for a given $A$ may be obtained by multiplying $A$ by the $\mu$ of the isotope in question and reading the graph at $a$. Allowances must also be made for the amount of activity involved and the average energy of the beta particles.

*Thin Source*: The curves in Figure 4*b*

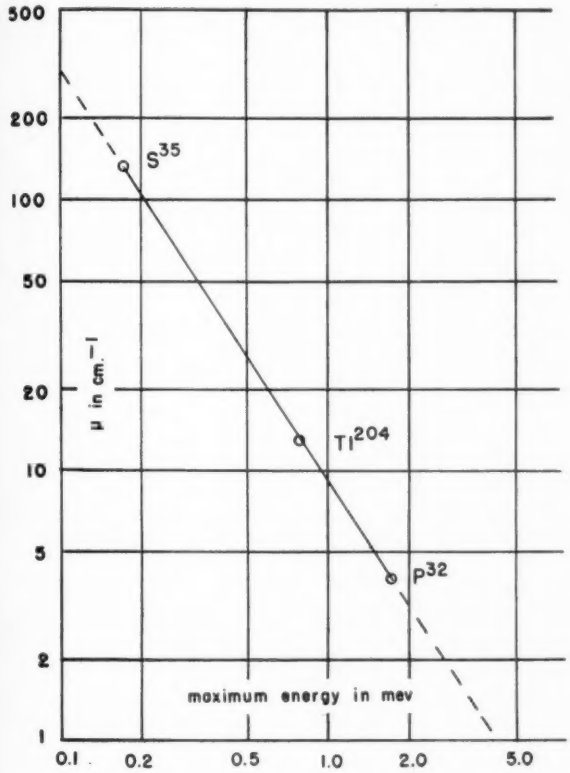


FIG. 3. Average absorption coefficient $\mu$ as a function of maximum beta energy. The three isotopes investigated by Baily are shown by circles. The straight line joining the points is given by $\mu = 8.8\ E^{-1.53}$.

apply to the geometry given in Figure 4*a*. They represent the dose as a function of distance from an infinite thin slab containing the activity. It should be noted that here again, as in all other examples, the absorption and scattering of beta particles are the same in the surroundings as in the source, *i.e.*, the curve applies to a homogeneous medium in which there is a uniform concentration of the radioisotope in an infinite layer.

The parameters characterizing this situation are

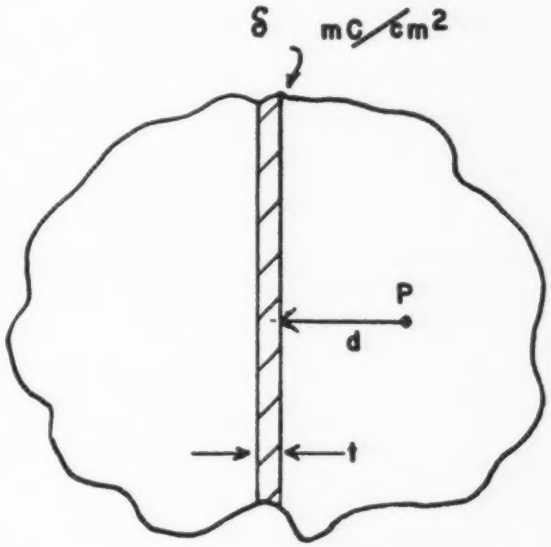


FIG. 4*a*. Geometry for dose from thin slabs with activity expressed in mc/cm.²

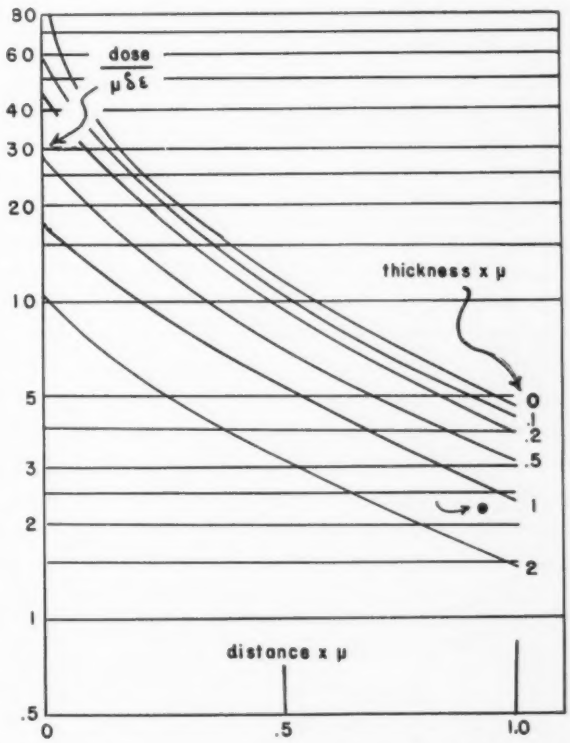


FIG. 4*b*. Dose as function of distance from slabs of various thickness. The scale of the ordinate is adjusted to yield equivalent roentgens per minute if $\mu$ is expressed in reciprocal centimeters, $\delta$ in mc/cm.² and $\epsilon$ in mev.

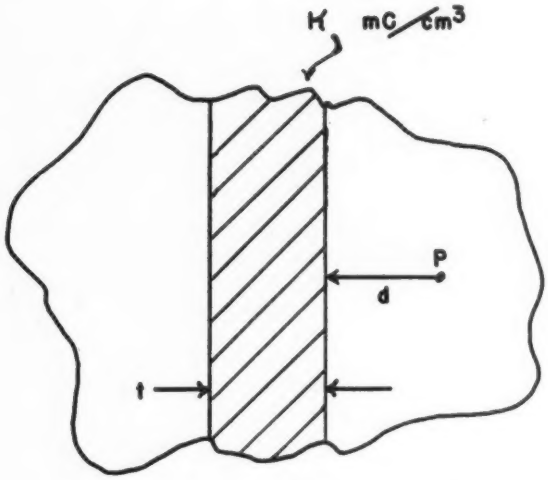


FIG. 5*a*. Geometry for doses from thick slabs with activities expressed in mc/cm.[3]

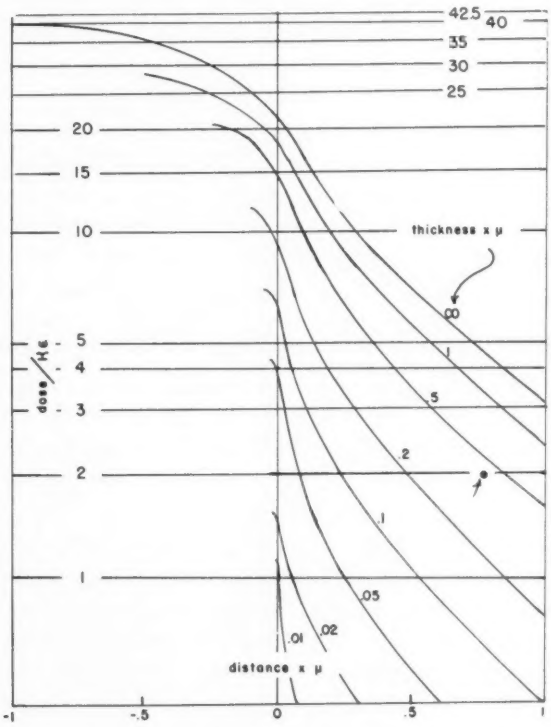


FIG. 5*b*. Dose as a function of distance from slabs of various thicknesses. The scale of the ordinate is adjusted to yield equivalent roentgens per minute if $\mu$ is expressed in reciprocal centimeters $\kappa$ in mc/cc., and $\epsilon$ in mev.

$t$, the thickness of the source in centimeters

$d$, the distance from the surface of the source in centimeters

$\delta$, the amount of beta activity per unit area of the source in millicuries/cm.$^2$

$\mu$, the absorption coefficient in reciprocal centimeters

$\epsilon$, the average beta-ray energy in mev.

To find the dose for a given situation, determine $\mu$ from Figure 3, multiply $t$ by $\mu$ to select an appropriate curve on Figure 4*b*, multiply $d$ by $\mu$ and read the ordinate corresponding to that value.

The dose in equivalent roentgens per minute (e.r./min.) will be equal to the

$$\text{ordinate} \times \mu \times \delta \times \epsilon$$

Consider for instance an experiment in which a salt containing $S^{35}$ has been soaked into a piece of filter paper at a concentration of 8 mc/cm.$^2$ The filter paper is 0.01 cm. thick, has a backing of some light plastic, and is applied to the skin. What will be the dose at the basal layer at a depth of 0.007 cm. (7 mg/cm.$^2$)?

The maximum beta-ray energy of $S^{35}$ is 0.17 mev. and hence (Fig. 3) $\mu$ is 133. Thus $t\mu = 1.33$ and $d\mu = 0.93$. These values determine a point on Figure 4b which is at the location indicated by the arrow. The corresponding ordinate is 2.2. Since the average beta energy of $S^{35}$ is 0.055 mev., the dose will be given by

$$2.2 \times 133 \times 8 \times 0.055 = 130 \text{ e.r./min.}$$

*Thick Slabs.* The above result could also have been obtained from Figure 5*b* which gives doses for sources for which the activity per unit volume is known. This family of curves includes one of infinite thickness, which could not be shown in Figure 4*b*.

The parameters here are (Fig. 5*a*): $\mu$, $\epsilon$ and

$t$, the thickness of the source in cm.

$d$, the distance from the surface of the source cm. (Note that this quantity is negative if the dose inside the source is to be determined.)

$\kappa$, the amount of beta activity per unit volume of the source in millicuries/cc.

The dose is determined in the same manner as in the previous example except that it will be given by the

$$\text{ordinate} \times \kappa \times \epsilon$$

Consider a flat beta applicator of 1 mm. thickness which contains $P^{32}$ at a concentration of 3 mc/cc. in a medium having approximately unit density (*e.g.*, bakelite). Suppose the dose at 2 mm. depth in tissue is to be determined.

$E_{max}$ for $P^{32}$ is 1.7 mev. Therefore $\mu$ is 4 cm.$^{-1}$ (Fig. 3). Hence $t\mu = 0.4$ and $d\mu = 0.8$. It will be seen from Figure 5*b* that these values yield an ordinate of 2.0. Since the average beta-ray energy of $P^{32}$ is 0.695 mev., the dose rate will be

$$3 \times 2.0 \times 0.695 = 4.2 \text{ e.r./min.}$$

*Spherical Sources.* While the theoretical dosimetry for slabs may be checked by comparison with experimental values, no measurements seem to be available for spheres. However, there seems to be reason

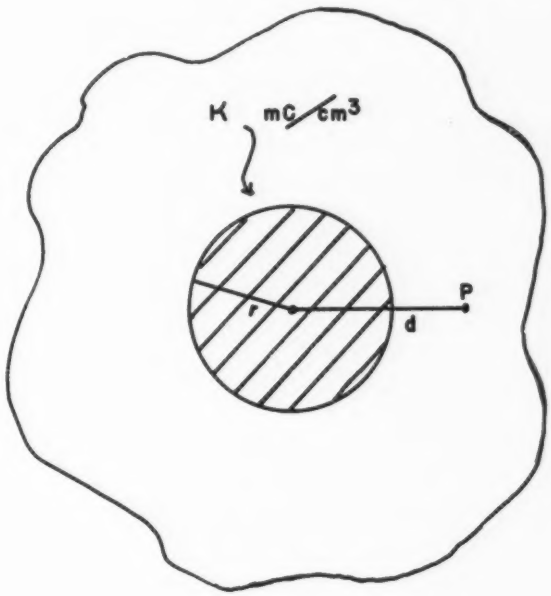


Fig. 6*a*. Geometry for dose from a sphere.

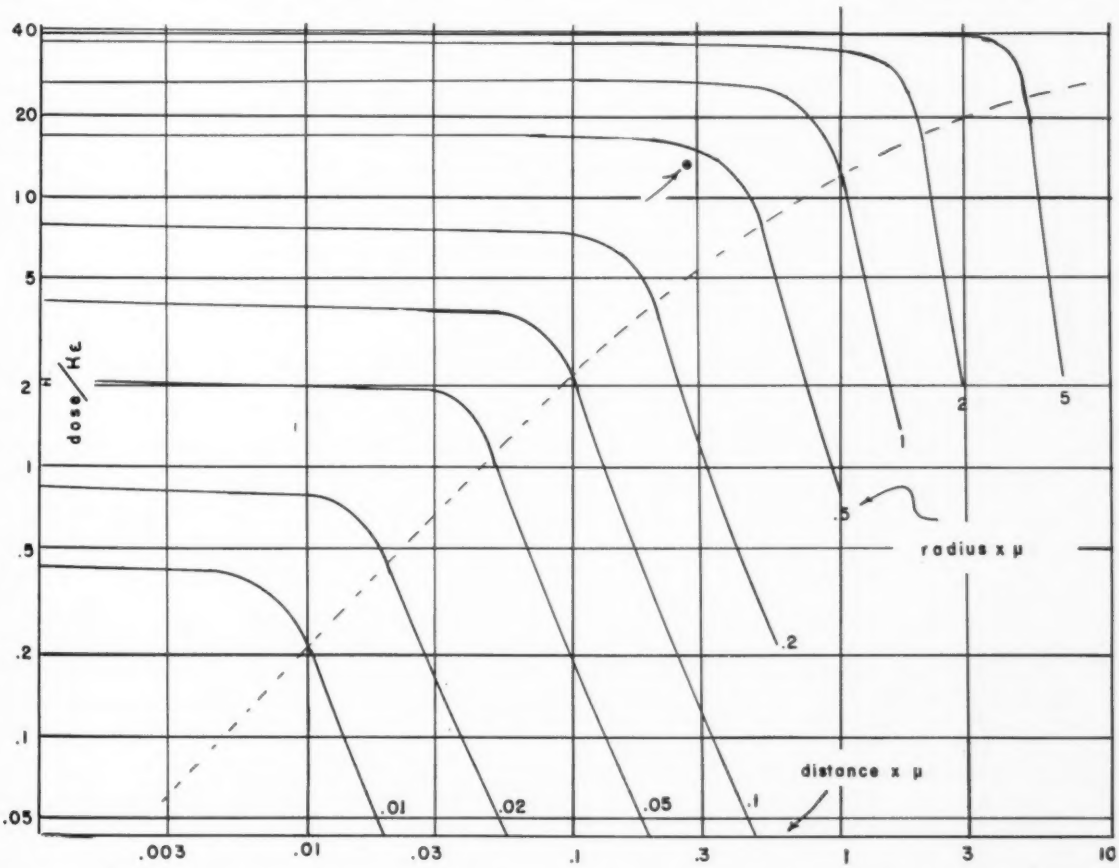


Fig. 6*b*. Dose as a function of distance from the centers of spheres of various radii. The scale of the ordinate is adjusted to yield equivalent roentgens per minute if $\mu$ is expressed in reciprocal centimeters, $\kappa$ in mc/cc. and $\epsilon$ in mev.

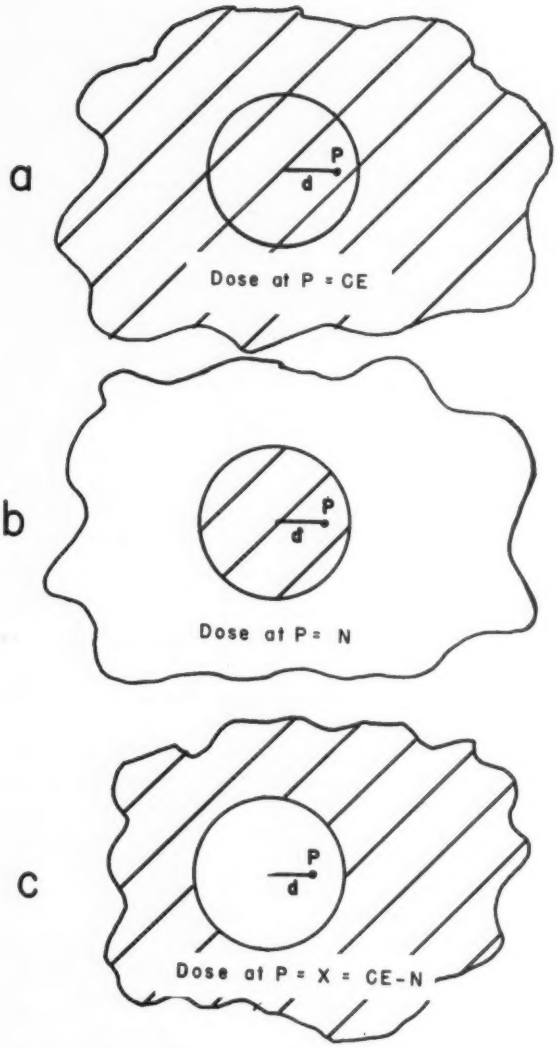


FIG. 7. Geometrical considerations for inverse dose.

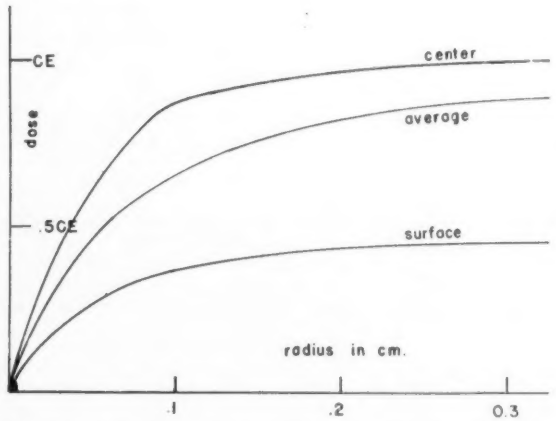


FIG. 8. Relative maximum, average, and minimum doses in spheres containing $I^{131}$ as a function of radius.

to assume that computations are about equally accurate in both instances. The sphere appears to be the only finite object which may be treated with reasonable effort in these computations. Its special significance lies in the fact that of all shapes it is the one in which there is a maximum of self-absorption. Therefore, if any irregularly shaped body containing the beta emitter is approximated by a sphere of equal volume, the dose received by the latter represents an upper limit of the emitted energy which may be retained in the original structure. Similarly, if an object of a given volume is immersed in a radioactive solution the average dose will be a minimum if the object is spherical.

The parameters involved in the dose from spherical sources are (Figure 6*a*): $\mu$, $\kappa$, $\epsilon$ and

$r$, the radius of the source in centimeters

$d$, the distance from the center of the source in centimeters. (This will be less than $r$ if the dose inside the source is to be computed.)

The dashed line in Figure 6*b* intersects the dose curves at $d=r$ and yields the dose on the surface of the spheres involved. Values to the left of the dashed line are doses inside the spheres, values to the right, doses outside the spheres.

The dose in e.r. is again given by the ordinate $\times \kappa \times \epsilon$.

As an example, one might consider a frog egg stripped of its jelly which is, by gentle stirring, made to float in a volume of water containing a beta emitter. This is a case of an "inverse dose." Assuming that none of the radioactive material diffuses into the egg, one is dealing with the dose in a spherical cavity in a large volume of radioactive material rather than a spherical source in a large inactive volume. If the egg were permeated with the activity at the same concentration as exists in the surrounding fluid, any point in it would receive *CE*, the dose in a continuum (Fig. 7*a*). This may be considered to be due to the dose *N* contributed by the active material inside the egg (Fig. 7*b*) plus the dose *X* contributed by active material outside the

egg (Fig. 7*c*). Thus $CE=N+X$ or $X=CE-N$. In the units employed here

$$CE=42.5\kappa\epsilon \text{ e.r./min.}$$

Suppose that the egg is immersed in a volume of water containing 0.5 mc/cc. of $Na^{24}$, that its diameter is 1.7 mm., and that this yields a dose rate of 8 e.r./min. This computation does not take into account the dose due to gamma rays emitted by $Na^{24}$.

A simple numerical integration of data in Figure 6*b* will yield the average dose received by active spherical objects in

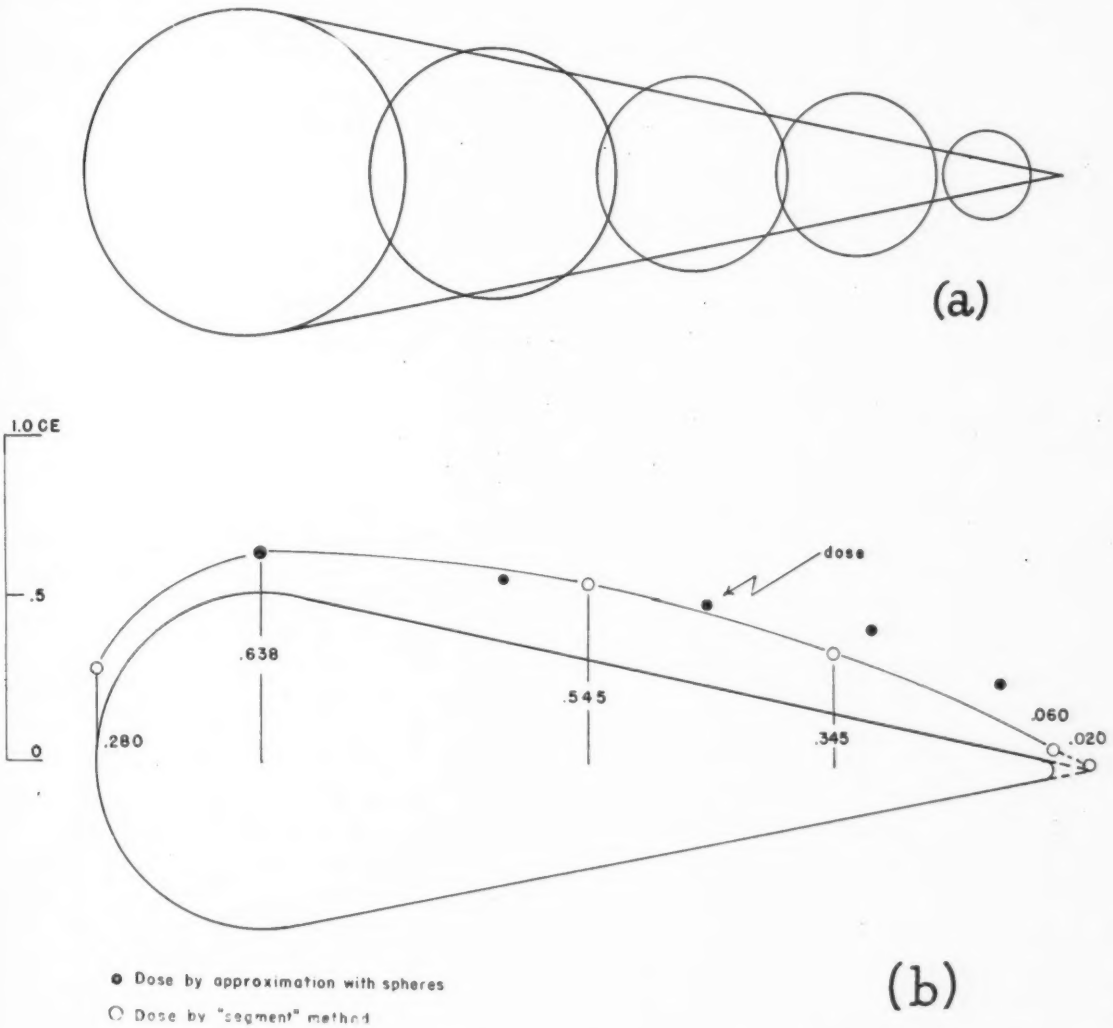


Fig. 9. Dose in the mouse thyroid. (*a*) Approximation used to determine dose. (*b*) Values obtained by approximation (solid circles) as compared with numerical integration (open circles).

the dose at a point 0.5 mm. from the center is to be determined.

$E_{max}$ for $Na^{24}$ is 1.4 mev. Therefore $\mu$ is 5.4 (Fig. 3). Thus $r\mu=0.46$ and $d\mu=0.27$. According to Figure 6*b*, this yields $N=13\kappa\epsilon$. Thus $X=CE-N=42.5\kappa\epsilon-13\kappa\epsilon=29.5\ \kappa\epsilon$. With $\epsilon$ for $Na^{24}$ being 0.54 mev., inactive media. This has been done for spheres of various sizes in Figure 8 for $I^{131}$. In this case there are two beta rays which must be treated separately. The curves indicate that there is a critical size for functional metastases of thyroid carcinomas. Even if the metastasis picks up the

iodine at the same rate as the original tumor, it will be irradiated less effectively if its radius is less than about 1 mm., because most of the beta rays escape and lose their energy in the surrounding tissues.

The examples thus far given involve only simple geometrical shapes and the question arises how more complicated objects may be analyzed.

Figure 9*a* shows a method whereby the dose in a non-spherical object may be determined by approximating the distribution of activity by overlapping spheres. Here the drop-shaped object approximates the shape of the mouse thyroid. To obtain the dose, the object is broken up into five overlapping spheres. In this modification of the geometry, excessive dose values would be obtained in those regions where the spheres overlap, but the dose at the center of each sphere may be obtained by adding to its own contribution the dose due to the other four. If the spheres approximate the original shape well, as on the left side of the figure, fairly accurate values will be obtained. This is shown in Figure 9*b* where the axial variation of dose as obtained in such a computation is compared with the results of a more laborious but more accurate numerical integration.

This method of approximation may in principle be applied to any shape, but it is likely that the labor involved would often be considerable and that sufficient information may be obtained by assuming a spherical shape for the object. Thus, while the study of the mouse thyroid as outlined above yields an average dose of somewhat less that 0.40 *CE*, the average dose in a sphere of the same mass would be 0.55 *CE*. Thus, even for fairly elongated shapes, the average dose differs not too much from the one encountered in a sphere of equal mass.

The authors wish to acknowledge with appreciation their indebtedness to Dr. G. Failla, who suggested many of these problems, the cooperation of Mr. Norman A. Baily of this laboratory, who made available the experimental data shown in Figure 2 and many helpful suggestions by Dr. Charles D. Swartz.

Calculations forming the basis of the dosimetric curves originally appeared in *Nucleonics* (July and August, 1950). The editors kindly gave permission to reproduce Figures 2, 4*b*, 5*b*, 6*b*, and 9.

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# DISTRIBUTION AND DOSAGE OF RADIOCARBON IN THE TISSUES*

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COMPOUNDS tagged with radiocarbon ($C^{14}$) promise to be versatile tools in the investigation of metabolic phenomena. However, because of the long half-life (5,000+years) of $C^{14}$ and the experiments of Bloom *et al.*,[1] suggesting that this element localizes in bone, there has been an understandable hesitation in the use of this element for human investigation.

If it could be shown that $C^{14}$ were rapidly excreted and evenly distributed through the body tissues, this useful agent might then be used with a minimum of hazard in selected clinical cases. The following experiment was carried out with this in mind.

1.728 mg. of glycine labeled with $C^{14}$ in the methylene position, having an activity of 567,000 counts per minute per milligram (4.57 $\mu$c/mg.) was injected intravenously into a series of mice. The animals were sacrificed at varying intervals from six hours to forty-three days and the individual tissues and organs combusted, plated, and counted as described by Calvin *et al.*[2] Activity in the carcass, expired air, urine, and feces was determined to eliminate sources of error. The total activity in each tissue analyzed expressed as percentage of the injected dose is shown in Table I.

Dr. William Siri in this laboratory has estimated the doses delivered to organs on the basis of values obtained in this experiment. Assuming a 70 kg. man the maximum r.e.p./day delivered to the various organs is shown in Table II.

SUMMARY

Radiocarbon ($C^{14}$) administered intravenously in the form of radioglycine is rapidly excreted from and evenly distributed in the tissues of mice. There is no evidence of bone localization. Calculated

TABLE I

PERCENTAGE OF ADMINISTERED DOSE OF $C^{14}$ REMAINING IN TISSUES

| Time | Bone | Brain | Heart | Intestine | Kidney | Liver | Stomach | Spleen | Pancreas | Colon | Lungs |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 6 hr. | 2.0 | 0.3 | 0.04 | 10.0 | 4.9 | 14.0 | 3.0 | 9.0 | 5.0 | 1.2 | 1.4 |
| 18 hr. | 0.5 | 0.5 | 0.04 | 6.0 | 3.0 | 6.7 | 4.3 | 2.0 | 1.5 | 8.5 | 1.4 |
| 25 hr. | 1.3 | 0.5 | — | 6.0 | 2.9 | 17.0 | 2.3 | 0.9 | 2.3 | 6.6 | 1.4 |
| 41 hr. | 1.0 | 0.3 | 0.5 | 9.0 | 2.5 | 12.0 | 3.4 | 1.9 | 1.0 | 1.5 | 0.3 |
| 68 hr. | 0.5 | 0.2 | 0.4 | 2.3 | 1.9 | 9.0 | 1.0 | 0.7 | 0.8 | 2.8 | 0.5 |
| 96 hr. | 0.6 | 0.5 | 0.4 | 5.5 | 2.1 | 8.0 | 0.7 | 0.5 | 0.5 | 2.6 | 0.6 |
| 6 days | 0.5 | 0.3 | 0.4 | 2.2 | 1.8 | 5.3 | 0.6 | 0.4 | 0.6 | 1.0 | 0.6 |
| 12 days | 0.25 | 0.3 | 0.1 | 1.0 | 0.7 | 2.0 | 0.2 | 0.25 | 0.3 | 0.4 | 0.2 |
| 14 days | 0.25 | 0.3 | 0.2 | 1.0 | 0.6 | 2.2 | 0.3 | 0.2 | 0.3 | 0.3 | 0.2 |
| 17 days | 0.3 | 0.3 | 0.2 | 0.3 | 0.6 | 1.4 | 0.15 | 0.2 | 0.2 | 0.4 | 0.2 |
| 21 days | 0.1 | 0.2 | 0.2 | 0.3 | 0.3 | 0.6 | 0.1 | 0.1 | 0.1 | 0.2 | 0.1 |
| 26 days | 0.1 | 0.1 | 0.1 | 0.2 | 0.2 | 0.6 | 0.07 | 0.15 | 0.08 | 0.2 | 0.1 |
| 34 days | 0.1 | 0.1 | 0.09 | 0.2 | 0.2 | 0.3 | 0.02 | 0.07 | 0.06 | 0.1 | 0.1 |
| 43 days | 0.05 | 0.1 | 0.05 | 0.08 | 0.05 | 0.2 | 0.04 | 0.04 | 0.1 | 0.07 | 0.04 |

* The work described in this paper was sponsored by the Atomic Energy Commission.

† While on leave from Massachusetts General Hospital, Boston, Massachusetts; Milton Fellow, Harvard University.

Table II

CALCULATED DAILY RADIATION TO TISSUES IN MAN IN R.E.P./DAY/MC.

| Tissue | 1st Day | 43rd Day |
|---|---|---|
| Bone | 0.13 | 0.005 |
| Brain | 0.015 | 0.003 |
| Heart | 0.05 | 0.005 |
| Kidney | 0.12 | 0.0002 |
| Liver | 0.14 | 0.0014 |
| Spleen | 0.65 | 0.002 |
| Pancreas | 0.5 | 0.022 |
| Lung | 0.12 | 0.0025 |
| Alimentary tract (Whole intestine) | 0.09 | 0.001 |

radiation to the individual tissues is minimal.

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# ON THE USE OF ROENTGEN FILMS IN DOSIMETRY

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IT HAS been pointed out to the author that films do not enjoy wide usage in dosimetry, particularly for roentgen radiation up to 400 kv. (peak). The reason appears to be that film sensitivity changes rapidly with quality and, of course, the quality would change considerably for relatively moderate changes in any material in the roentgen-ray beam.

This laboratory, on the other hand, has been working in the 20 million volt region and has found quite a different behavior. It is the purpose of this note to mention a property of some roentgen films which is believed to be useful in dosimetry.

Our experience began during the war when the roentgenographic properties of various commercial roentgen films were being investigated. It was noticed that, under certain conditions, the photographic density exhibited by the film increased linearly with exposure from about twice the fog value up to at least density = 4. Three films, Eastman Industrial Types A

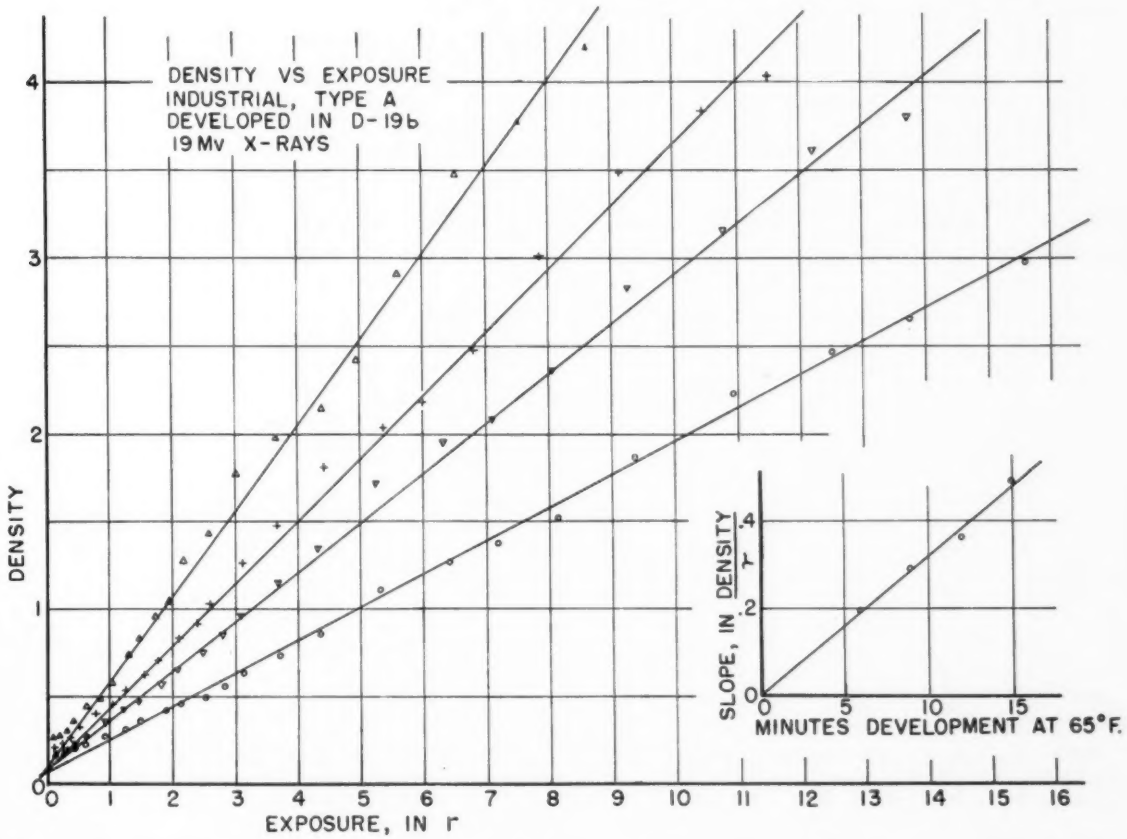


FIG. 1. Dose-Density Curve. The dose (exposure) is measured in roentgens. The film cassette contained a 0.040 inch lead screen between film and target. As normally defined, the contrast $\gamma = \Delta D/\Delta \log E = E\Delta D/\Delta E$ increases linearly with both dose and development. Increasing the contrast by, say, overdevelopment can be very useful in studying the details of multiple beams cross-firing on a common target. The dose values (abscissae) must be divided by 3.0 to obtain the number of roentgens which would be observed at the film position.*

* The reason for this factor is that the ionization chamber could not be at the film position while the tests were in process.

and M and Eastman No Screen, behaved this way when a lead screen (0.040 inch was used most) was placed in the cassette and between the film and target. A back lead screen would not change this but is roentgenographically poor practice. The roentgenographic results are published elsewhere.[1,2] Figure 1 shows a typical plotting of density *vs.* exposure, the exposure having been measured in terms of the reading of a Victoreen thimble when irradiated in a thick-walled bakelite cylinder. The thick wall is necessary in the 20 million volt range to approach the equilibrium condition involved in the definition of the roentgen (r).

Linearity of response was not always retained when fluorescent screens were used but otherwise seemed to be a property of these emulsions. Film used in a paper cassette[3,4] was employed widely for relative dosimetry in one case treated in this laboratory. Figure 5 of reference 4 illustrates the kind of linearity which was found under experimental and processing conditions which were more carefully controlled than in the roentgenographic work. In fact, there is some reason to believe that with sufficiently well controlled conditions, such films as those mentioned above might be useful for absolute as well as relative dosimetry. This would at least require a calibration for each box.

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# MEASUREMENT OF THE NECK OF THE FEMUR

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THE common orthopedic practice of maintaining reduction of fractures of the femoral neck by means of a Smith-Petersen or similar nail has made the preoperative determination of the length of the neck of the femur a roentgenographic procedure of considerable value to the orthopedic surgeon. Knowing the exact length of the femoral neck permits the orthopedist to preoperatively select with certainty a nail of appropriate length, thus securing maximum stability of fragments

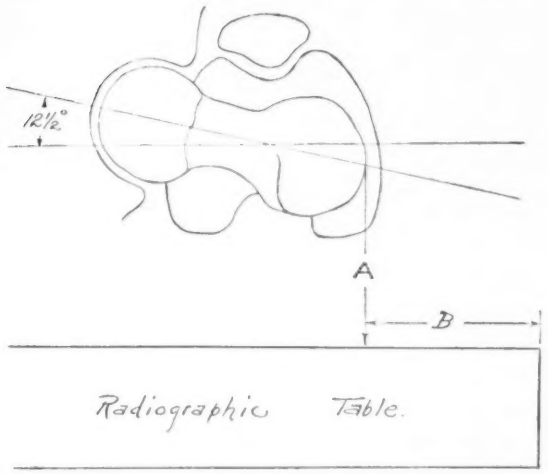


FIG. 1. Diagram to show the normal anterior angulation of the femoral neck and measurements taken to properly position perforated lead plate.

and avoiding the possibility of unnecessary osseous trauma due to withdrawing a nail found to be too long or too short and replacing it with one of proper length.

It is the purpose of this paper to describe a simple apparatus and technique by which the length of the femoral neck may be determined accurately at the time of the first roentgenological examination without discomfort to the injured patient or appreciably prolonging the time of the examination.

To determine and record the length of the femoral neck use is made of a perforated lead plate, following a modification of the roentgenographic method of measurement believed to have been first described by Thoms.[1]

The femora being normally bilaterally symmetrical and seldom showing any appreciable difference in the length of the right and left femoral neck, measurement is made of the uninjured femur.

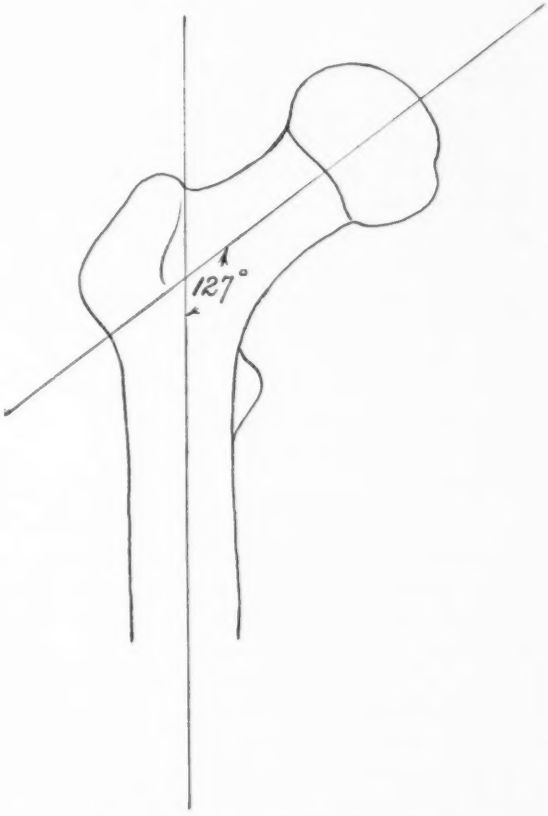


FIG. 2. Diagram to show the angle normally present between the femoral neck and the long axis of the shaft of the femur.

Since the neck of the femur normally angles anteriorly 12.5 degrees and forms an angle of 127 degrees with the long axis of the shaft of the femur, as shown in Figures 1 and 2, it is necessary that the perforated lead plate must not only be positioned at

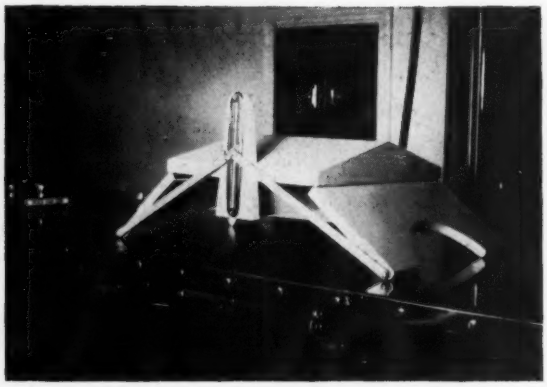

FIG. 3. Apparatus to support the perforated lead plate at a previously determined distance above the roentgenographic table.

the same distance from the film as was formerly occupied by the neck of the femur, but must also be positioned to conform to the anterior angulation of the femoral neck. For the sake of accuracy and convenience it is of value to place the rows of perforations in the plate at an angle of 127 degrees to conform to the normal angle of the femoral neck with the long axis of the shaft of the femur.

The apparatus designed to support the perforated lead plate at the same distance from the film and at the same angle as the femoral neck is shown in Figure 3. It consists of a platform of wood or suitable radiolucent material, readily adjustable in height, and made to cover a surface of 14 by 17 inches. The surface of the platform forms an obtuse angle so that when placed upon the roentgenographic table with the long dimension across the table both sides slope downward at an angle of 12.5 degrees, corresponding to the normal anterior angulation of the femoral neck. Upon this platform the perforated lead plate is placed. For purposes of protection the perforated plate is covered with plywood.

Because the orthopedic nails used in fractures of the femoral neck are usually made varying in length by fractions of an inch, the perforations of the lead plate are placed $\frac{1}{2}$ inch apart and arranged in rows at an angle of 127 degrees. The arrangement of the perforations is indicated by the dots produced upon the film shown in Figure 4.

The procedure followed in performing a roentgenographic examination of a patient suspected of having a fracture of the neck of the femur is as follows: The patient is placed upon the roentgenographic table in a supine position. Care is taken that the following conditions are met: (1) The patient is centered in the middle of the table. (2) The pelvis is flat, having its transverse axis parallel with the surface of the table. (3) The uninjured leg is positioned so that the foot is pointed directly upward and maintained in this position by means of sandbags or other suitable support. With the patient thus positioned upon the table, the lateral aspect of the greater trochanter of the uninjured femur is palpated and two measurements carefully taken and recorded. These measurements are the height of the lateral aspect of the greater trochanter above the surface of the roentgenographic table (distance *A*, Fig. 1) and the distance from the edge of the roentgenographic table to a point on the surface of the table directly below the lateral aspect of the greater trochanter (distance *B*, Fig. 1).

Following the taking of these measurements a pair of 14 by 17 inch stereoscopic anteroposterior films are made at a known target-film distance showing the bony pelvis and the proximal ends of the femora. The tube is shifted in the direction of the long axis of the table.

The film made with the tube in its first position is then developed and examined. If a fracture of the femoral neck is present, a lateral film is made. As soon as the film in the lateral projection is made the patient is taken from the roentgenographic table and may be removed from the roentgen department.

The tube is now returned to the same height and position it occupied in making the second of the stereoscopic anteroposte-

Fig. 4. Fracture of the neck of the femur. Roentgenogram with dots for accurate measurement of the length of the femoral neck.

rior films and the undeveloped film is again placed in position beneath the table. The perforated lead plate is placed upon the table over the exposed but undeveloped film and its height adjusted so that the perforated plate lies in the same position with relation to the film as was occupied by the uninjured femoral neck at the time of the exposure of the film. This is easily accomplished by adjusting the elevating mechanism so that the height of the plate above the table at distance *B* from the edge of the table is the same as distance *A*. With the perforated plate so positioned a second exposure is made producing rows of dots upon the film. Since the distance between the dots in any row on the film represents $\frac{1}{2}$ inch, the length of the femoral neck is easily determined and a nail of proper length selected prior to operation.

The presence of the small dots on one of the stereoscopic films has not been found to interfere significantly with the stereoscopic viewing of the films. Should they be found, however, to be a disturbing influence to any roentgenologist, an additional special film may, of course, be made for purposes of measurement.

The errors in measurement which may result from difficulty in determining the exact position of the lateral aspect of the greater trochanter due to overlying soft tissues and from slight anatomical variations in the degree of anterior angulation of the neck of the femur have not been found in practice to be of sufficient magnitude to interfere with the clinical usefulness of the procedure.

SUMMARY

Apparatus and a technique have been described by which the length of the femoral neck may be measured. The purpose of this measurement is to permit the preoperative selection of a Smith-Petersen or similar nail of proper length for each individual case of fracture of the femoral neck.

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# EDITORIALS

## CATARACT FORMATION FOLLOWING WHOLE BODY IRRADIATION

THE effect of whole body irradiation on the lens, and the ocular structures in general, has become a topic of intensive investigation since the atomic explosions at Hiroshima and Nagasaki. The problem is fraught with considerable difficulty since the irradiation in such explosions is usually due to several agents as, for example, gamma rays, neutrons, radioactive fission products, etc., all of which have various energies and thus produce different biologic effects. To simplify the analysis, it appears advisable to consider separately the acute or immediate lenticular changes which are observed as the result of lethal doses of whole body irradiation and the chronic or delayed lenticular changes culminating in cataract formation which are the product of sublethal doses and, as a rule, occur several years later. In these latter, a distinction may be made between cataracts due to single exposure to an instantaneous dose and cataracts due to repetitive exposure to small doses over a certain period of time.

Experimentally, the acute or immediate lenticular changes were studied by Wilder and Maynard,[1] who took part in Operation Crossroads at Bikini. These investigators exposed 21 goats and 31 pigs to varying amounts of whole body irradiation emanating from an atomic explosion and compared the changes observed in this group of animals with those found in 24 pigs subjected to whole body roentgen irradiation with 200 to 600 r and 24 control animals. All heavily and moderately irradiated animals of the Bikini experiment died within three to twenty-three days following exposure from radiation sickness except 2 which were killed by exsanguination, one on the sixth and the other on the eighth day. Of 7 animals which received lesser radiation, 3 died and 4 were killed, the longest period of observation being 184 days. The animals subjected to roentgen irradiation and the control animals likewise died or were killed at varying intervals over a period of seven months. Wilder and Maynard state that the pathologic lesions of the eye in the animals which received whole body irradiation, whether from atomic bomb explosion or roentgen rays, consisted of conjunctival and intraocular hemorrhages, intraocular serous exudates, septic choroiditis and the presence of bacteria in the intraocular blood vessel. These lesions were attributed to bone marrow depression and secondary infection rather than to direct effect of the irradiation. The changes observed in the lens constituted part of the total picture. Five lenses from heavily irradiated animals, 2 from the atomic explosion group and 3 from the roentgen experiment group, showed extensive degeneration, but most of the other animals showed minimal alterations. In the roentgen experiment group, several of the pigs were pregnant at the time of the irradiation and the eyes of 2 fetuses from one of the sows which received 400 r and of 2 fetuses from another sow which received 600 r were examined. Massive degenerative changes were found in all four lenses of the fetuses from the sow which received 600 r, although the mother showed only early posterior subcapsular degeneration of the lens. Prominent changes were also present in the four lenses of the 2 fetuses from the sow which received 400 r but this mother exhibited small vacuoles in the cortex of the

[1] Wilder, Helenor Campbell, and Maynard, Russell M. Ocular changes produced by total body irradiation. *Am. J. Path.*, Jan.–Feb., 1951, *27*, 1–19.

lens. Similar vacuoles, however, were observed in many of the other irradiated animals, as well as in some of the controls, and therefore Wilder and Maynard believe that they do not represent a specific manifestation of the direct effect of irradiation. The disproportionately greater degenerative changes observed in the lenses of the fetuses are undoubtedly due to the fact that the irradiation occurred when the tunica vasculosa lentis was still present, thus injuring the blood supply at the time of most rapid growth of the lens. This finding is in agreement with former observations on increased susceptibility to cataract formation of newborn animals following local roentgen irradiation of the eyes.[2]

Reports on the acute or immediate effect on the lens of human beings by whole body irradiation produced by atomic explosion are few. Tamura and his co-workers[3] studied the lenticular changes in forty-eight eyes from atomic bomb victims at Hiroshima and Nagasaki who died of a severe radiation sickness. They found vacuoles in the lens fibers of six eyes, localized in the equatorial sections of the lens. In two of these lenses there was evidence of degeneration of the center with swelling and disintegration of a thin layer of cortex beneath the anterior and posterior capsules. Schlaegel,[4] in 1947, described the histopathologic changes of six eyes and one other lens from 7 patients who died at Kyushu Imperial University. The most conspicuous findings were thickening of the posterior capsule and the presence of multiple vacuoles in the anterior and posterior subcapsular cortex which he interpreted as being due to anoxia although the possibility of early cataract formation was conceded. Wilder,[5] in examining sixteen lenses of eyes of atomic bomb casualties from Hiroshima, found in fifteen of them degenerative changes consisting of swelling of fibers at the posterior pole and large vacuoles beneath the capsule.

In considering the chronic or delayed lenticular changes resulting from whole body irradiation, some benefit may be derived from reviewing briefly some of the available data on the effect of local irradiation of the lens by roentgen rays or radium. Such information has been gathered since the earliest days of the therapeutic use of these two agents. Numerous experimental investigations have been performed, especially in rabbits, since this animal has a large crystalline lens and can be handled easily in the laboratory. Other animals studied were cats, guinea pigs, mice and a few larger animals, such as dogs and pigs. Through the years, approximately one hundred cases of incidental cataracts were also reported in human beings, usually subsequent to irradiation of ocular or orbital lesions. The literature dealing with the various phases of the subject up to 1931 was extensively reviewed by Desjardins.[6] Owing to the rather indefinite methods of dosage measurement prevailing at that time, however, no precise figures could be compiled as regards the amounts of radiation necessary to produce the cataract. Neither was it possible to determine the relative effect of the two types of radiation.

During the past decade several notable contributions were published giving more accurate data. Thus, Poppe[7] found that in adult rabbits the smallest cataractogenic dose for single local roentgen exposure with 175 kv. was 250 r. Clinically observable opacities appeared beneath the posterior capsule within five to seven months after irradiation and persisted to the end of the observation (nineteen months after irradiation). Cogan and Donaldson[8] also reported

[2] Bellows, J. G. Cataract and Anomalies of the Lens. C. V. Mosby Company, St. Louis, 1944, pp. 323–377.

[3] Tamura, S., Ikui, H., Nakano, K., Hiwatashi, T., and Oshio, S. Ocular lesions from the atomic bomb. *Ganka Rinsho Iho*, 1946, *5*, 40, and *6*, 90. (Cited by Kimura and Ikui.[11])

[4] Schlaegel, T. F., Jr. Ocular histopathology of some Nagasaki atomic-bomb casualties. *Am. J. Ophth.*, 1947, *30*, 127–135.

[5] Wilder, H. C. Pathology of the eye in atomic bomb casualties. (Abstract.) *Am. J. Path.*, 1947, *23*, 890.

[6] Desjardins, A. U. Action of roentgen rays and radium on the eye and ear. Am. J. Roentgenol. & Rad. Therapy, 1931, *26*, 639–679; 787–819; 921–942.

[7] Poppe, Erik. Experimental investigations of the effects of roentgen rays on the eye. Pp. 102, with xv plates. I. Kommisjon Hos Jacob Dybwad, Oslo, 1942.

[8] Cogan, David G., and Donaldson, David D. Experimental

a threshold cataractogenic dose of 250 r in ten week old rabbits for 200 kv. and 1,200 kv. roentgen rays. This uniformity is interesting since the threshold dose for epilation amounted to 900 r for 175 kv. in Poppe's experiments and to 1,000 r for 200 kv. and 1,500 r for 1,200 kv. in Cogan and Donaldson's experiments. These latter authors state, categorically, that the lens is a relatively susceptible organ to irradiation and that the threshold dose for production of cataract is smaller than that for a grossly demonstrable effect on any other structure of the eye or periocular region. They further state that with larger doses the latent period of the cataract is an inverse function of the dose and of the age.

Poppe[7] also studied the effect of repetitive local roentgen exposure on the crystalline lens of rabbits. In one series of animals he administered daily doses of 175 to 250 r, up to a total dose of 400 to 2,500 r, and in another series small separate doses at prolonged intervals up to a total dose of 750 to 1,050 r. He found that in both instances the lenticular changes were somewhat less pronounced than after single exposure with the same total dose, but the difference was not so great as in the cornea, conjunctiva and hair papillae. Likewise, the reparative ability of the lens was much less, when compared with that of the other structures. The latent period between irradiation and the clinical appearance of the cataract was somewhat longer.

The threshold value of the cataractogenic dose for human beings is unknown. The individual cases recorded in the literature usually received rather large doses but it is conceivable that cataracts might have resulted from considerably smaller amounts of radiation under identical circumstances. Hunt,[9] after a detailed analysis of the available information and a retrospect study of 5 personal cases (2 irradiated with roentgen rays and 3 with gamma rays of radium), states that the threshold dose of radiation productive of lenticular opacities appears to be about 1 skin unit. He observed cataract formation following single delivery of 775 r tissue dose (about 1.5 skin units) with 130 kv. (peak) and of about 1,000 gamma roentgens (1 skin unit) to the lens. The cataract appeared from six months to eight and more years after irradiation. Cogan and Donaldson[8] likewise state that the probable cataractogenic dose of roentgen rays of 100 kv. energy or greater is somewhere between 500 and 1,000 r and that the younger the person, the greater the susceptibility. With repetitive and protracted irradiation the dose is somewhat larger.

The more recent studies on the chronic or delayed lenticular changes due to whole body irradiation include survey of the incidence of cataracts in the survivors of the atomic explosion of Hiroshima and Nagasaki who received a single instantaneous exposure, and an analysis of several reports on accidental cataracts discovered in persons working with ionizing radiations who were victims of repetitive exposures over a prolonged period of time.

The frequency of the late radiation cataracts in the population of Hiroshima and Nagasaki was investigated by Cogan, Martin and Kimura[10] at the suggestion of the Committee on Ophthalmology of the National Research Council under the auspices of the Atomic Bomb Casualty Commission. Ten cases of cataracts believed to have been caused by atomic radiation were found, 9 at Hiroshima and 1 at Nagasaki. All were within 550 to 950 meters of the hypocenter at the time of explosion and suffered epilation of the head after one to four weeks, with complete baldness lasting three to seven months. Six vomited on the day of explosion and 8 had fever, malaise and diarrhea lasting from one to three weeks. The failure of vision, which was either gradual or stepwise and fluctuant, started in one patient one month, in another six months and in the remainder two

radiation cataracts. I. Cataracts in the rabbit following single x-ray exposure. *A.M.A. Arch. Ophth.*, May, 1951, *45*, 508–522.

[9] Hunt, Howard B. Cancer of the eyelid treated by radiation; with consideration of irradiation cataract. AM. J. ROENTGENOL. & RAD. THERAPY, 1947, *57*, 160–180.

[10] Cogan, David G., Martin S. Forrest, and Kimura, Samuel J. Atom bomb cataracts. *Science*, 1949, *110*, 654–655.

and one-half years after the bombing. The cataracts, at the time of the survey, consisted of opacities of the posterior lenticular capsules with occasional punctate dots farther toward the periphery, being approximately symmetrical in the two eyes. There were vacuoles just in front of the capsules and in the 2 most advanced cases the opacity centrally was separated into two laminae which toward the periphery fused to form a denser ring in the shape of a doughnut. The pattern and the progression of the cataracts, according to Cogan, Martin and Kimura, were similar to those associated with exposure to roentgen and gamma rays. The part played by the neutrons in their production is unknown but must have been significant. These authors also state that examination of 1,000 persons, believed to represent a cross section of the survivors who were within 2,000 meters of the hypocenter, revealed no case of radiation cataract.

Kimura and Ikui[11] reported somewhat later that in 1 of the aforementioned 10 persons an intracapsular cataract extraction was successfully performed on one lens about four years after exposure to the atomic bomb, with good restoration of vision. It thus appears that the retina and other structures of the eye were not damaged by the radiation.

As regards the possible occurrence of late radiation cataracts secondary to repetitive small exposures over a prolonged period, the publication of Abelson and Kruger[12] is illuminating. These authors state that, following discovery that at least 5 nuclear physicists of average age thirty-one were afflicted with incipient cataracts, an ad hoc committee has been set up by the Division of Medical Sciences of the National Research Council for the purpose of surveying the situation. Arrangements were made to have the afflicted men examined and on January 18, 1950, it was found that of 11 men examined 10 showed opacities in the lenses. Three exhibited severe changes in the posterior cortex of the lens, consisting of thick saucer or disc-like densities associated with slight subcapsular or anterior cortical haze; 4 had similar changes of a lesser degree; and the remaining 3 showed minimal or doubtful changes, consisting of a thin lacy opacity in the posterior cortex and occasional punctate dots or capsular iridescence. All of the men were exposed to cyclotron radiation, the principal components of which were neutron and gamma rays, with the former predominating. Abelson and Kruger state that the pattern of the changes conformed to that observed in roentgen-ray and radium cataracts. The exact calculation of the dosage proved a rather difficult task but, even with due regard to the higher biologic effectiveness of the neutrons as compared to the roentgen and gamma rays, the cumulative doses estimated were surprisingly low with a median dose of only 50 n. Most of the men had periodic blood examinations at the time they were receiving the exposure but not in a single case was there any evidence of abnormality, perhaps due to the fact that the upper segment of the body was principally implicated in the neutron irradiation. In only 2 instances was there a mild epilation. The fully developed cataracts appeared three years after the radiation was received. In 2 men they were successfully removed soon thereafter, and the vision restored.

Hempelman, Lisco and Hoffman,[13] in publishing the results of a collaborative clinical investigation and the case histories of 9 persons who were injured during two accidental nuclear reactions at the Los Alamos Scientific Laboratory, also make mention of a thirty-four year old man who developed bilateral radiation cataracts. This man was 3 feet away from the experimental assembly when the accident oc-

[11] Kimura, Samuel J., and Ikui, Hiroshi. Atomic bomb radiation cataract; case report with histopathologic study. *Am. J. Ophth.*, June, 1951, *34*, 811–816.

[12] Abelson, P. H., and Kruger, P. G. Cyclotron-induced radiation cataracts. *Science*, 1949, *110*, 655–657.

[13] Hempelman, Louis H., Lisco, Hermann, and Hoffman, Joseph G. The acute radiation syndrome; study of nine cases and a review of the problem. *Ann. Int. Med.*, Feb., 1952, Part 1, 279–510, with xxiv plates.

curred and, being partially shielded and turned slightly to the left, received most of the exposure to his head, shoulders and left arm. The average dose to his body was calculated to have been equivalent to 390 r of 80 kv. roentgen rays and 26.4 r of gamma rays. Seventeen days after exposure, he developed epilation of the left temple and face which cleared up completely within five months. Three years later a cataract of the left eye was noted, followed within two years by a cataract of the right eye.

Recently, Cogan, Donaldson and Reese[14] reviewed the clinical findings in 20 cases of radiation cataract which they have examined. Of these, 10 cases represented the group studied in Japan to which reference has already been made above, 1 case had a cataract resulting from an atomic explosion in this country, 2 cases had cyclotron-induced cataracts and 7 cases developed cataracts following local exposure to roentgen and gamma rays during the course of therapeutic application. The findings were remarkably uniform in all cases, whether the cataract was a sequel of whole body irradiation or of a local exposure. The conspicuous features were (1) a doughnut-shaped configuration, as demonstrated ophthalmoscopically, and (2) a bivalve configuration with sharply demarcated anterior boundary of the opacity, as seen with the slit-lamp biomicroscope. Although these features are not entirely specific, according to Cogan, Donaldson and Reese their presence is strongly suggestive of radiation cataract and usually permits a differentiation from posterior polar cataract, such as is observed with retinitis pigmentosa, and the so-called cataracta complicata, commonly associated with endogenous ocular lesions and systemic diseases, and often occurring without apparent cause.

[14] Cogan, David G., Donaldson, David D., and Reese, Algernon B. Clinical and pathological characteristics of radiation cataract. *A.M.A. Arch. Ophth.*, Jan., 1952, *47*, 55–70.

Cogan, Donaldson and Reese[14] also studied the histopathologic characteristics of radiation cataracts. The material used for this study consisted of the lenses obtained from 27 cases, in 2 of which the cataract was caused by the ionizing effect of the atomic bomb (including the case of Kimura and Ikui[11]), in 1 it was induced by cyclotron exposure and in 24 it had resulted from local roentgen therapy or radium application for neoplasms in or about the eye. In general, the histopathologic manifestations of the radiation cataract also assumed a rather uniform pattern but the type specificity was less pronounced than in the case of the clinical signs. The essential changes consisted of (1) failure of the cells at the equator to differentiate into lens fibers, and (2) early migration of cells beneath the posterior capsule toward the posterior pole, leading to occasional thickening of the posterior capsule before any extensive changes had occurred in the cortex.

In summarizing, it may be said that the acute or immediate lenticular changes resulting from lethal or near lethal doses of whole body irradiation constitute part of a general effect. The chronic or delayed changes, culminating in cataract formation, are due to the particular radiosusceptibility of the crystalline lens. Whether the exposure is single or repetitive and whether it extends to the entire body or only the head region, the clinical and histopathologic pattern of the cataract is identical with that observed following local exposure of the eye to roentgen rays or radium. Newer evidence, however, seems to indicate that the cataractogenic threshold dose is lower than heretofore assumed and that cataracts may develop especially following small repeated exposures, without any outward sign or hematologic warning of damaging radiation effect. Fortunately, such cataracts may be removed with good restoration of vision.

T. LEUCUTIA, M.D.

# ISAAC GERBER
## 1885-1952

DR. ISAAC GERBER, one of the most distinguished radiologists in New England, died of coronary occlusion at the age of sixty-six in Providence, Rhode Island, on February 17, 1952. He was born in Boston, graduated from Harvard Medical School in 1910 and, after serving his internship, went to Europe for a two-year period of graduate study in internal medicine. While abroad, however, he became interested in radiology and decided to devote his whole time to the new branch of medicine. On his return to Boston in 1913, he joined the office of a pioneer radiologist, the late Dr. Arial W. George, and presently found himself engaged in a round of conferences and lectures, introducing and interpreting radiology to the profession at large. His

approach must have been impressive since, as he told me, Rhode Island physicians soon urged him to establsh an office in Providence. He did so in 1914, was appointed chief of radiology at Rhode Island Hospital shortly afterwards and in due course became consultant to virtually every other hospital in the state. Many of his investigative studies—on the gallbladder, appendix, duodenum, mastoids, lungs, dental radiology, on radiation treatment of neoplasms and of a variety of benign lesions—were published during those years. He organized the radiologic service of Massachusetts' famed cancer hospital in Pondsville at its inception. His work, by then, had become authoritative. He had materially helped to give radiology its place in clinical medicine. He was in his early forties.

It was at this point that disease slowly began to cripple his legs with paralysis, finally shackling him to a wheelchair for the last fifteen years of his life. The illness was a mystery to the neurologists and was at times ascribed to radiation damage. It could have been cured. At autopsy the pathologist found a benign neurofibroma compressing the cord.

Isaac Gerber's struggle against infirmity was on an epic scale. With the devoted support of his wife, Rose Albert Gerber, a scholar in her own right and a woman of charm and courage, he continued all his activities. For many years the short sturdy man in the wheelchair remained a familiar sight at conferences and at nearly all regional and national meetings. To watch him at work, upright on his helpless legs, holding on to the fluoroscope with one hand and competently operating a spot-film device with the other, was an experience not easily forgotten.

Ike Gerber practiced radiology as one should practice it but rarely does. At his busy office he or his long-time partner, Dr. Simon Albert, saw every patient first and took a history, no matter how obvious or trivial the problem. The work had an accuracy and thoroughness which I have not seen matched. A "simple" wrist examination required routinely six specified views, and he could give a valid reason for each of them, reminiscing briskly and with grim relish about the errors he had made by omitting one or the other. What he called "the a.p. and lateral school of thought" headed the list of his dislikes. He inspected the day's films at the office, then leisurely at home, wary of hunches, collecting and sifting the evidence. The next morning, he reviewed them again, inviting and visibly enjoying a good argument but dissecting promptly, though impersonally, opinions that were not based on observation checked and confirmed. It was characteristic of him that once, when I helped him for a few weeks during World War II, he suddenly interrupted one of our endless film-reading sessions, bellowing, at nobody in particular, "There is altogether to much agreement in this office today!"

Experience, clinical research, prodigious reading and a lasting interest in all aspects of medicine had given him an encyclopedic knowledge of radiology which his reticence rarely permitted him to display. It was probably this knowledge which led him to set standards of completeness and precision which the rest of us have been slow to adopt. In this respect he was ahead of his time.

Although fiercely averse to publicity, he was given positions of trust and leadership in the community and was, of course, highly respected by the profession. He was a member of the American Roentgen Ray Society, a past president of the New England Roentgen Ray Society, a Fellow of the American College of Radiology, and a member of numerous other national associations.

As our field expands and our position improves, we are beginning to forget that radiology owes its present standing to the inquisitiveness and stamina of a very few. Among them, Isaac Gerber will be remembered as a master for his competence, his honesty, his valor, but mainly perhaps for his insistent belief that in medicine the best is barely good enough and that with thought and effort one can make the best a little better—commonly at least, as he would here have added.

ALBERT OPPENHEIMER, M.D.

# SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

## MEETINGS OF ROENTGEN SOCIETIES*

### United States of America

**American Roentgen Ray Society**
*Secretary*, Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Pa. Annual meeting: Shamrock Hotel, Houston, Texas, September 23, 24, 25 and 26, 1952.

**American Radium Society**
*Secretary*, Dr. J. E. Wirth, 635 Herkimer St., Pasadena 1, Calif. Annual meeting: Stevens Hotel, Chicago, Ill., June 8, 9 and 10, 1952.

**Radiological Society of North America**
*Secretary*, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y. Annual meeting: Netherland-Plaza Hotel, Cincinnati, Ohio, December 7 to 12, 1952.

**American College of Radiology**
*Executive Secretary*, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Illinois.

**Section on Radiology, American Medical Association**
*Secretary*, Dr. T. Leucutia, Harper Hospital, Detroit 1, Mich. Annual meeting: Chicago, Ill., June 9–13, 1952.

**Alabama Radiological Society**
*Secretary*, Dr. J. A. Meadows, Jr., Medical Arts Bldg., Birmingham 5, Ala. Meets time and place Alabama State Medical Association.

**Arizona Radiological Society**
*Secretary*, Dr. R. Lee Foster, 507 Professional Building, Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

**Arkansas Radiological Society**
*Secretary*, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

**Atlanta Radiological Society**
*Secretary*, Dr. J. D. King, 35 Linden Ave., N.E., Atlanta, Ga. Meets monthly, except during three summer months, on second Friday evening.

**Brooklyn Roentgen Ray Society**
*Secretary*, Dr. J. J. Daversa, 345 75th St., Brooklyn, N. Y. Meets monthly fourth Tuesday, October through April.

**Buffalo Radiological Society**
*Secretary*, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

**Central New York Roentgen Ray Society**
*Secretary*, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

**Central Ohio Radiological Society**
*Secretary*, Dr. F. A. Riebel, 15 West Goodale St., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Columbus Athletic Club, Columbus, Ohio.

**Chicago Roentgen Society**
*Secretary*, Dr. B. D. Braun, 6 N. Michigan Ave., Chicago 2, Ill. Meets second Thursday of each month, October to April inclusive at the University Club.

**Cleveland Radiological Society**
*Secretary*, Dr. Mortimer Lubert, 10515 Carnegie Ave., Cleveland 6, Ohio. Meetings at 6:45 P.M. on fourth Monday of each month from October to April.

**Colorado Radiological Society**
*Secretary*, Dr. W. P. Stampfli, 1933 Pearl St., Denver, Colo. Meets third Friday of each month at University of Colorado Medical Center or at Denver Athletic Club.

**Connecticut Valley Radiologic Society**
*Secretary*, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday October and April.

**Dallas-Fort Worth Roentgen Study Club**
*Secretary*, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

**Detroit Roentgen Ray and Radium Society**
*Secretary*, Dr. J. C. Cook, Harper Hospital, Detroit, Mich. Meets monthly first Thursday, October to May, at Wayne County Medical Society Building.

**East Bay Roentgen Society**
*Secretary*, Dr. Dan Tucker, 434 30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

**Florida Radiological Society**
*Secretary*, Dr. Nelson T. Pearson, 1109 Huntington Bldg., Miami, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

**Georgia Radiological Society**
*Secretary*, Dr. R. C. Pendergrass, Americus, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

**Greater Miami Radiological Society**
*Secretary*, Dr. Maurice Greenfield, Ingraham Bldg., Miami, Fla. Meets third Wednesday of each month at Veterans Administration Building.

**Houston Radiological Society**
*Secretary*, Dr. F. M. Windrow, 1205 Hermann Professional Bldg., Houston, Texas. Meets fourth Monday each month.

**Idaho State Radiological Society**
*Secretary*, Dr. Alfred M. Stone, St. Lukes Hospital, Boise, Idaho. Meets annually at same time as Idaho State Medical Association.

**Illinois Radiological Society**
*Secretary*, Dr. Stephen L. Casper, 1101 Maine St., Quincy, Ill. Meets three times a year.

**Indiana Roentgen Society**
*Secretary*, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

**Iowa X-Ray Club**
*Secretary*, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society.

**Kansas Radiological Society**
*Secretary*, Dr. Charles M. White, 3244 E. Douglas, Wichita 8, Kan. Meets annually with State Medical Society.

**Kentucky Radiological Society**
*Secretary*, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

**Kings County Radiological Society**
*Secretary*, Dr. Marcus Wiener, 1430 48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

**Los Angeles Radiological Society**
*Secretary*, Dr. John B. Hamilton, 210 N. Central Ave., Glendale 3, Calif. Meets second Wednesday each month at Los Angeles County Medical Association Building.

**Louisiana Radiological Society**
*Secretary*, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

**Maine Radiological Society**
*Secretary*, Dr. C. F. Miller, Central Maine General Hospital, Lewiston, Maine.

* Secretaries of societies are requested to send timely information promptly to the Editor.

MIAMI VALLEY RADIOLOGICAL SOCIETY
*Secretary*, Dr. G. A. Nicoll, 134 Apple St., Dayton, Ohio. Meets second Friday of fall and winter months.

MID-HUDSON RADIOLOGICAL SOCIETY
*Secretary*, Dr. J. W. Walton, Horton Memorial Hospital, Middletown, N. Y. Meets 8:30 P.M., fourth Tuesday each month, September to May.

MILWAUKEE ROENTGEN RAY SOCIETY
*Secretary*, Dr. T. J. Pfeffer, 839 N. Marshall St., Milwaukee 2, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
*Secretary*, Dr. L. A. Nash, 572 Lowry Medical Arts Bldg., St. Paul 2, Minn. Meets three times annually, once at time of State Med. Assn., and in spring and fall.

MISSISSIPPI RADIOLOGICAL SOCIETY
*Secretary*, Dr. John W. Evans, 621 High Street, Jackson 2, Miss. Meets third Thursday of each month at the Rotisserie Restaurant at 6:30 P.M.

NASSAU RADIOLOGICAL SOCIETY
*Secretary*, Dr. Joseph J. La Vine, 259 North Grand Ave., Baldwin, N. Y. Meets second Tuesday of the month in February, April, June, October and December.

NEBRASKA RADIOLOGICAL SOCIETY
*Secretary*, Dr. R. W. Blanchard, 1216 Medical Arts Bldg., Omaha, Nebr. Meets fourth Thursday of each month at 6 P.M. at Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
*Secretary*, Dr. L. L. Robbins, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Harvard Club.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
*Secretary*, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
*Secretary*, Dr. Irving Schwartz, 45 E. 66th St., New York 21, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
*Secretary*, Dr. J. E. Hemphill, 1420 E. Fifth St., Charlotte 4, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
*Secretary*, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings by announcement.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY
*Secretary*, Dr. John F. Roach, Albany Hospital, Albany, N. Y. Meets on the second Wednesday of October, November and March at the University Club, Albany. Annual meeting in June to be announced.

NORTHERN CALIFORNIA RADIOLOGICAL CLUB
*Secretary*, Dr. G. A. Fricker, Sacramento County Hospital, Sacramento, Calif. Meets at dinner last Monday, every second month, except June, July and August.

OHIO STATE RADIOLOGICAL SOCIETY
*Secretary*, Dr. Willis S. Peck, 2001 Collingwood Blvd., Toledo, Ohio.

OKLAHOMA STATE RADIOLOGICAL SOCIETY
*Secretary*, Dr. W. E. Brown, 2020 S. Xanthus, Tulsa 4, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
*Secretary*, Dr. J. Richard Raines, 214 Medical-Dental Bldg., Portland 5, Oregon. Meets monthly from October to June on the second Wednesday of each month at 8:00 P.M. at the University Club.

ORLEANS PARISH RADIOLOGICAL SOCIETY
*Secretary*, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
*Secretary*, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
*Secretary*, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
*Secretary*, Dr. J. M. Converse, 416 Pine St., Williamsport.

PHILADELPHIA ROENTGEN RAY SOCIETY
*Secretary*, Dr. G. P. Keefer. American Oncologic Hospital, Philadelphia 4, Pa. Meets first Thursday each Month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
*Secretary*, Dr. E. J. Euphrat, 3500 Fifth Ave., Pittsburgh 13, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
*Secretary*, Dr. Richard B. Hanchett, 705-6 Medical Arts Bldg., Baltimore, Md. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
*Secretary*, Dr. Fred. Zaff, 135 Whitney Ave., New Haven, Conn. Meets bimonthly on second Wednesday.

RADIOLOGICAL SECTION, MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA
*Secretary*, Dr. U. V. Wilcox, 915 Nineteenth St., N. W., Washington 6, D. C. Meets Medical Society Library, third Thursday of January, March, May and October at 8:00 P.M.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
*Secretary*, Dr. Roy G. Giles, Temple, Texas.

RADIOLOGICAL SOCIETY OF GREATER CINCINNATI
*Secretary*, Dr. Lee S. Rosenberg, Jewish Hospital, Cincinnati 29, Ohio. Meets first Monday each month, October through May.

RADIOLOGICAL SOCIETY OF HAWAII
*Secretary*, Colonel Alexander O. Haff, M.C., Tripler Army Hospital, Honolulu, T. H. Meets third Friday of each month at Tripler Army Hospital.

RADIOLOGICAL SOCIETY OF KANSAS CITY
*Secretary*, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

RADIOLOGICAL SOCIETY OF NEW JERSEY
*Secretary*, Dr. Nicholas G. Demy, 912 Prospect Avenue, Plainfield, N. J. Meets annually at Atlantic City at time of State Medical Society and mid-winter at Elizabeth, N. J.

RICHMOND COUNTY RADIOLOGICAL SOCIETY
*Secretary*, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
*Secretary*, Dr. George Gamsu, 191 S. Goodman St., Rochester, N. Y. Meets monthly on last Monday from September through May, 8:00 P.M. at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
*Secretary*, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr. Mid-Summer Conference, Shirley-Savoy Hotel, Denver, Colo., August 7, 8 and 9, 1952.

ST. LOUIS SOCIETY OF RADIOLOGISTS
*Secretary*, Dr. Francis O. Trotter, Jr., 634 N. Grand Blvd., St. Louis 3, Mo. Meets fourth Wednesday each month, except June, July, August and September.

SAN DIEGO RADIOLOGICAL SOCIETY
*Secretary*, Dr. Rex Uncapher, 7720 Girard Ave., La Jolla, Calif. Meets first Wednesday of each month at the University Club.

SAN FRANCISCO RADIOLOGICAL SOCIETY
*Secretary*, Dr. I. J. Miller, 2680 Ocean Avenue, San Francisco 27, Calif. Meets quarterly.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
*Secretary*, Dr. D. R. MacColl, 2007 Wilshire Blvd., Los Angeles 5, Calif.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
*Secretary*, Dr. Harold L. Shinall, St. Joseph's Hospital, Bloomington, Ill.

SHREVEPORT RADIOLOGICAL CLUB
*Secretary*, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

SOUTH BAY RADIOLOGICAL SOCIETY
*Secretary*, Dr. Ford Shepherd, 526 Soquel Avenue, Santa Cruz, Calif. Meets second Wednesday each month.

South Carolina X-Ray Society
*Secretary*, Dr. Henry E. Plenge, Spartanburg General Hospital, Spartanburg, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

Tennessee Radiological Society
*Secretary*, Dr. J. M. Frère, Newell Hospital, Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
*Secretary*, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Next meeting: San Antonio, Texas, January 23 and 24, 1953.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital.

University of Wisconsin Radiological Conference
*Secretary*, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

Utah State Radiological Society
*Secretary*, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

Virginia Radiological Society
*Secretary*, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
*Secretary*, Dr. John N. Burkey, 555 Medical-Dental Bldg., Seattle 1, Wash. Meets fourth Monday of each month from September through May.

Westchester Radiological Society
*Secretary*, Dr. Walter J. Brown, Northern Westchester Hospital, Mt. Kisco, N. Y. Meets on third Tuesdays of January and October and on two other dates to be announced.

Wisconsin Radiological Society
*Secretary*, Dr. Irving I. Cowan, 425 E. Wisconsin Ave., Milwaukee 2, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-Ray Study Club of San Francisco
*Secretary*, Dr. Charles E. Duisenberg, Palo Alto Clinic, 300 Homer Ave., Palo Alto, Calif. Meets third Thursday at 7:45 P.M., January to June, Lane Hall, Stanford University Hospital; July to December, San Francisco Hospital.

## Cuba, Mexico and Central America

Sociedad de Radiología y Fisioterapia de Cuba
*President*, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Sociedad Mexicana de Radiologia y Fisioterapia
*General Secretary*, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

Sociedad Radiológica Panameña
*Secretary*, Dr. L. Arrieta Sanchez, Apartado No. 86, Panama, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

## British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1.

Faculty of Radiologists
*Honorary Secretary*, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
*Honorary Secretary-Treasurer*, Dr. Jean Bouchard, Suite 305, 1555 Summerhill Avenue, Montreal 26, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
*Secretary*, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française d'Électrologie et de Radiologie Médicales
*Secretary*, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

Australian and New Zealand Association of Radiologists
*Honorary Secretary*, Dr. Alan R. Colwell, 135 Macquarie St., Sydney, N.S.W.
*Honorary Secretaries*, State Branches:
New South Wales, Dr. E. W. Frecker, 135 Macquarie St., Sydney.
Victoria, Dr. T. L. Tyrer, 3 Lockerbie Court, East St. Kilda.
Queensland, Dr. J. Adam, 131 Wickham Terrace, Brisbane.
South Australia, Dr. R. deG. Burnard, 170 North Terrace, Adelaide.
Western Australia, Dr. A. M. Nelson, 179 B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

## South America

Asociacion Argentina de Radiologia
*Secretary*, Dr. Lidio G. Mocsa, Avda. Gral Paz 151, Córdoba, Argentina. Meetings held monthly.

Sociedad Argentina de Radiologia, Junta Central, Buenos Aires
*Secretary*, Dr. Oscar F. Noguera, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

Sociedad Argentina de Radiologia, Filial del Litoral, Sede, Rosario
*President*, Dr. Francisco P. Cifarelli. Meets monthly second Wednesday, 19 ha 663 Italia St., Rosario, Santa Fe.

Sociedad Argentina de Radiologia, Filial del Sur, Sede, La Plata
*President*, Prof. Dr. Jose P. Uslenghi, La Plata. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Centro, Sede, Cordoba
*President*, Prof. Dr. David L. Caro, Corro 86, Cordoba. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Norte, Sede, Tucuman
*President*, Dr. Julio Mendez Valladares, Rivadavia 358, Tucuman. Meets monthly.

Sociedad Argentina de Radiologia, Filial de Cuyo Sede, Mendoza.
*President*, Dr. J. A. Orfila, Hospital Central, Mendoza. Meets monthly.

Sociedade Brasileira de Radiologia Medica
*Secretary*, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
*Secretary*, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Colombiana de Radiologia
*Secretary*, Dr. Alberto Torres Focke, Av. 34, No. 17–34, Bogota, Colombia. Meets last Wednesday of each month.

Sociedad Peruana de Radiologia
*Secretary*, Dr. Julio Bedoya Paredes, Apartado 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
*Secretary*, Dr. Arias Bellini, Av. Agraciada 1464, Piso 13, Montevideo, Uruguay.

### Continental Europe

**Société Belge de Radiologie**
*General Secretary*, Dr. S. Masy, 111 Avenue des Allies, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

**Société Française d'Electro-Radiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord**
*Secretary-General*, Dr. A. Dariaux, 9 bis, Boulevard Rochechouart, Paris IX$^{e}$, France.

**Ceskoslovensk společnost pro rëntgenologii a Radiologii v Praze**
*Secretary*, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

**Polish Society of Radiology**
*Secretary*, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland.

**Gdansk Section, Polish Society of Radiology**
*Secretary*, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10:30, X-Ray Dept., Akademia Gdansk.

**Warsaw Section, Polish Society of Radiology**
*Secretary*, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

**Societatea Romana de Radiologie si Electrologie**
*Secretary*, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

**All-Russian Roentgen Ray Association, Leningrad**
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
*Secretaries*, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

**Scandinavian Roentgen Societies**
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

**Sociedad Espanola de Radiologia y Electrologia**
*Secretary*, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

**Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)**
*Secretary*, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

**Deutsche Roentgen-Gesellschaft**
*Secretary*, Dr. Peter Kröker, (22a) Essen-Helsingen, Westpreussenstrasse 21. Meets annually in different towns.

**Societa Italiana dr Radiologia Medica**
*Secretary*, Prof. Mario Ponzio, Ospedale Mauriziano. Torino, Italy. Meets biannually.

### India

**Indian Radiological Association**
*Secretary*, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

## ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

The Fourteenth Annual Mid-Summer Conference of the Rocky Mountain Radiological Society will be held in Denver, Colorado, at the Shirley-Savoy Hotel on August 7, 8, and 9, 1952.

The program, not yet completed, includes the following guest speakers. They and their titles are:

W. C. Banks, D.V.M., College Station, Texas
1. "Clinical Cases Occurring in Veterinary Radiology"
2. "Some Diseases of Dogs that also Occur in Man"

Philip J. Hodes, M.D., Philadelphia, Pennsylvania
1. "The Roentgen Manifestations of Pancreatic and Periampullary Disease"
2. "The Roentgen Manifestations of Cerebellopontine Angle Tumors"

Harold O. Peterson, M.D., St. Paul, Minnesota
1. "The Roentgen Diagnosis of Benign Gastric Ulcer"
2. "Unusual Neurologic Conditions with Diagnostic Roentgen Findings"

George H. Ramsey, M.D., Rochester, New York
1. "Cinefluorographic Analysis of Some Movements of the Cervical Spine"
2. "Cinefluorographic Analysis of the Causes of Dysphagia"

A. Justin Williams, M.D., San Francisco, California
"Roentgen Diagnosis of Intra-Abdominal Hernia"

A symposium on diseases of animals transmissible to man will be presented from the standpoint of veterinary medicine as well as from the bacteriological, pathological and clinical viewpoints.

A condensed schedule of the program includes the following titles to be presented by members and guests:

Richard B. Bridenbaugh, M.D., Billings, Montana
"Gallstone Ileus"

H. H. Dunham, M.D., Kansas City, Kansas
"Lymphosarcoma; A Review of One Hundred Cases"

William M. Kitchen, M.D., Kansas City, Missouri
"Examination of the Bleeding Colon"

Morris H. Levine, M.D., Denver, Colorado
"Beta Radiation of the Eye"

Gerald S. Maresh, M.D., Denver, Colorado
"Roentgen Therapy in Lymphoid Hyperplasis of the Nasopharynx"

H. Marks, M.D., New York, New York
"Palliative X-Ray Therapy with the Use of a Grid in Advanced Carcinoma"

J. R. Maxfield, Jr., M.D., Dallas, Texas
"Radioactive Iodine, $I^{131}$, as an Indicator of Thyroid Function and for the Therapy of Certain Thyroid Diseases"

J. Marshall Neely, M.D., Lincoln, Nebraska
"An Evaluation of Sella Turcica Changes, the Result of Intracranial Pathology"

Henry H. Plenk, M.D., Salt Lake City, Utah
"Aneurysmal Dilatation of the Great Vessels: The Use of Angiocardiography and Cardiac Catheterization in the Differential Diagnosis"

Marcus J. Smith, M.D., Santa Fe, New Mexico
"Roentgenographic Aspects of Complete and Incomplete Pulmonary Infection"

E. Dale Trout, Ph.D., Milwaukee, Wisconsin
"The Use of Filters to Control Patient Dose in Diagnostic Roentgenography"

C. Edgar Virden, M.D., Kansas City, Missouri
"Testicular Neoplasms"

Angus K. Wilson, M.D., Salt Lake City, Utah
"Investigations of Silicosis in Utah"

Round table discussions will be held in connection with luncheon meetings. Evening meetings will include a joint session with the Denver Medical Society, followed by Dutch lunch, and an informal banquet with entertainment. The annual picnic on Saturday afternoon will conclude the conference.

## INTERNATIONAL CONGRESS OF STRATIGRAPHY

The Second International Congress on Stratigraphy will be held in Genova, Italy, under the direction of Professor Alessandro Vallebona from September 1 to 10, 1952.

The course will be subdivided into two parts:

Part I (September 1–3), reserved for those who attended the first course held in

1950, in which subjects of general technique will be discussed.

Part II (September 4–10), for all participants, in which the improvement of the method during the past two years will be especially dealt with.

An invitation is extended to physicians and especially to Italian and foreign radiologists. The lectures will be given by Italian and foreign instructors.

The charge for Part I and Part II is L. 5000; for Part II, L. 3500.

Requests for the course, accompanied by payment, should be sent by May 30, 1952, to the secretary of the course, Dr. Alessandro Piazza, Istituto di Radiologia dell'Università di Genova, Ospedale San Martino, Genova, Italy.

### THIRD SYMPOSIUM NEURO-RADIOLOGICUM

The December, 1951, issue of the JOURNAL (page 980) carried an announcement of the Third Symposium Neuroradiologicum which will be held in Stockholm, Sweden, September 17–20, 1952. The preliminary program of the Symposium is now available. Leading specialists from Britain, Canada, France, Germany, The Netherlands, Italy and Sweden will read about 30 papers concerning the roentgen diagnosis of lesions of the brain and the spinal cord. Among the subjects to be discussed are:

Roentgenological diagnosis of spinal tumors
Vertebral angiography
Encephalography in tumor cases
Tomography in neuroradiology

Scientific and technical exhibitions are being arranged and a social program is planned.

Programs and application forms can be obtained from the Secretary of Symposium Neuroradiologicum, Serafimerlasarettet, Stockholm K, Sweden.

### AMERICAN COLLEGE OF RADIOLOGY

At the Twenty-eighth Annual Meeting of the American College of Radiology held in Chicago, Illinois, on February 8, 1952, Dr. John S. Bouslog, Denver, was elected *President* of the College for 1952–1953 and Dr. Robert P. Ball, Baton Rouge, *Vice-President;* Dr. John D. Camp, Los Angeles, *Chairman* of the Board of Chancellors, and Dr. Earl E. Barth, Chicago, *Treasurer*. Dr. Wilbur Bailey, Los Angeles, and Dr. Barton R. Young, Philadelphia, were elected to four year terms on the Board of Chancellors. Representing the scientific societies on the Board of Chancellors, Dr. Joshua C. Dickinson, Tampa, was elected to a one year term on the nomination of the American Roentgen Ray Society, and Dr. Arthur C. Singleton, Toronto, was elected to a two year term on the nomination of the Canadian Association of Radiologists.

At the annual banquet Dr. George E. Pfahler of Philadelphia was presented with the Gold Medal of the College of Radiology by President R. R. Newell. In presenting the Medal, President Newell stated that it was the eighth such award in the history of the College and briefly noted Dr. Pfahler's many contributions to the practice of medicine and the sp.cialty of radiology.

### IDAHO STATE RADIOLOGICAL SOCIETY

The formation of the Idaho State Radiological Society took place on June 19, 1951, during the meeting of the State Medical Association in Sun Valley, Idaho. The officers are as follows: *President*, Dr. Alfred Popma, Boise, Idaho; *Vice-President*, Dr. Judson B. Morris, Boise, Idaho; *Secretary-Treasurer*, Dr. Alfred M. Stone, Boise, Idaho.

Dr. Popma at this time was also elected President of the Idaho State Medical Association.

The meetings of the Idaho State Radiological Society are held annually in conjunction with those of the Idaho State Medical Association.

### NASSAU RADIOLOGICAL SOCIETY

The Nassau Radiological Society was formally organized on January 29, 1952, and a charter was adopted. The roster of

the Society includes nearly all of the qualified radiologists of Nassau and Suffolk Counties (New York State). The following officers were elected to serve for one year: *President*, Dr. Percival A. Robin, Hempstead, New York; *Vice-President*, Dr. James C. Barnett, Hicksville, New York; *Secretary*, Dr. Joseph J. La Vine, Baldwin, New York; *Treasurer*, Dr. David L. Jellinger, Patchogue, New York; *Executive Committee*, Dr. Herbert R. Zatskin, Greenvale, New York, and Dr. Benjamin L. Fuerstein, Bay Shore, New York.

The Society will meet on the second Tuesday of the month in February, April, June, October and December.

### RADIOLOGICAL SOCIETY OF HAWAII

The Radiological Society of Hawaii was formed March 14, 1952. Officers elected were: *Secretary*, Colonel Alexander O. Haff, M.C., Tripler Army Hospital, Honolulu, T.H.; *Treasurer*, Philip S. Arthur, M.D., Young Hotel Building, Honolulu, T.H. Meetings are held monthly on the third Friday at Tripler Army Hospital.

# ABSTRACTS OF RADIOLOGICAL LITERATURE

*Department Editor:* T. Leucutia, M.D., Harper Hospital, Detroit 1, Michigan

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## ROENTGEN DIAGNOSIS

### Abdomen

Gianturco, Cesare. Gastric double contrast. *South. M. J.*, June, 1951, *44*, 478–481.

When the author first began his work with the double contrast study of the stomach he advocated the use of a small amount of barium followed by an equal amount of mineral oil. The mineral oil separates the walls of the stomach so that they show a double contrast between them. Later, however, he noted that by reducing the amount of barium and utilizing the gas normally contained within the stomach, the mineral oil could be dispensed with in about 90 per cent of the patients.

His present procudure is to use 2 ounces of thick barium which is distributed over the mucosa of the stomach by palpation or positioning of the patient. The air bubble is then shifted about within the stomach, thus producing a double contrast in the various gastric areas.

When oil is being used several normal appearances may be confused and misinterpreted as pathological changes. Barium drops in oil may simulate an ulcer crater; large bubbles of oil or air may simulate polyps. In some instances, the mucosa may show a glandular appearance. This is due to small air bubble mixed with barium, mucus or saliva.

The double contrast method is particularly useful in those patients in whom the stomach is high and transverse in position or in whom segments of the stomach lie partially or completely beneath the costal border. It is stated in the article that this procedure is not intended to replace the studies made with pressure, but is suggested for supplementary examination when pressure cannot be adequately applied.

The demonstrable gastric changes are illustrated by diagrams and reproductions of typical roentgenograms.—*J. G. Snead, M.D.*

Hurwitz, Sidney, and McAlenney, Paul F. Trichobezoar in children; review of the literature and report of two cases. *Am. J. Dis. Child.*, June, 1951, *81*, 753–761.

Two cases of trichobezoar in children are reported with a review of the literature. Bezoars may be classified as (1) trichobezoars, or hairballs, which form the commonest type in man and are particularly common in the cow, horse and cat, especially during the hair-shedding season; (2) phytobezoars, which are composed chiefly of fruit and vegetable fibers, seeds and skins, the persimmon being most frequently involved; (3) trichophytobezoars, which are a mixture of animal hairs and vegetable fibers; and (4) concretions, which are bezoars of a harder, firmer and solider character (usually shellac) and are found in painters and furniture workers who have swallowed shellac solutions probably for alcholic content.

The symptoms of trichobezoar include pain, vomiting, constipation, alternating with diarrhea, foul breath, anemia, exhaustion and intolerance to solids. Roentgenography and gastroscopy are considered by the authors as the best means of establishing the diagnosis, and one or both should be employed in all instances of obscure gastrointestinal disturbance.

The treatment is surgical and the prognosis is excellent with early diagnosis, the mortality being less than 4 per cent. Death, when it occurs, is due to inanition, intestinal obstruction or perforation. The paper is illustrated with roentgenograms of the two cases.—*R. S. Bromer, M.D.*

Benson, Clifford D., and Coury, John J. Congenital intrinsic obstruction of the stomach and duodenum in the newborn. *Arch. Surg.*, June, 1951, *62*, 856–866.

A newborn infant with a prepyloric diaphragm successfully treated is described, the second to be reported in the literature. Ten patients with congenital intrinsic obstruction of the duodenum have been operated on and 7 have survived. Seven of these 10 patients were premature infants. Two of the deaths occurred in premature infants weighing less than 3 pounds (1.3 kg.). The other one involved a full term infant who died four days postoperatively after an anterior gastroenterostomy. Eight of the 11 infants were girls. Each of the 11 cases are briefly described and representative roentgenograms are reproduced.

In a review of this series of patients with congenital intrinsic obstruction of the stomach and duodenum, certain factors stand out as playing a major role in determining the morbidity and mortality rates. Prematurity was exhibited by 7 of the 11 patients operated on. For the classification of prematurity the authors used the standard of any infant whose birth weight is less than 2,500 gm. Of the 3 deaths in this entire series, 2 involved infants weighing less than 3 pounds (1.3 kg.).—*E. G. McDonald, M.D.*

Wood, Elizabeth C., and Smellie, J. M. Congenital hypertrophic pyloric stenosis; review of 320 cases. *Lancet*, July 7, 1951, *2*, 3–7.

This is a very complete report of the largest series of cases ever reported by English authors. The age and sex incidence agree closely with other large series.

Clinically, vomiting without anorexia but associated with weight loss and constiption were the outstanding symptoms. On physical examination, visible gastric peristalsis and a palpable pyloric tumor were the main features. In most cases the diagnosis was made from the clinical history and the physical findings.

Roentgenographic examination was used only infrequently. The authors feel that it should be used only in the doubtful case and stress that the characteristic shadow of barium in the narrowed pyloric canal must be constant and demonstrated on more than one film.

Three hundred, or 93 per cent, of the cases were treated surgically with only 5 deaths. All phases of the pre- and postoperative care as well as the complications are fully discussed.—*Norman Heilbrun, M.D.*

Walton, Franklin E. Surgical treatment of familial polyposis. *Arch. Surg.*, June, 1951, *62*, 833–846.

Familial polyposis of the colon is a specific clinical entity. The diagnosis and extent of the disease can be confirmed by means of contrast enemas. The symptoms and signs of this disease include bowel irregularity, diarrhea, the presence of mucus and blood in the stool and abdominal cramps and tenesmus. Any of these should warrant a digital rectal examination and a proctosigmoidoscopic examination, at which the polyps may be seen under direct vision and tissue removed with the biopsy forceps from characteristic and suspicious areas for microscopic section. In spite of a specific history and the majority of the above signs and symptoms, a certain number of proctosigmoidoscopic examinations will not reveal any suggestive lesion, and it remains for the contrast enema not only to clinch the diagnosis but in each instance to demonstrate the anatomical limitations and the extent of the disease. Inasmuch as the disease is a specific clinical entity, with a mendelian dominant which is transmitted by father or mother and may be inherited by children of either sex, it does not seem justifiable to consider the classification of Erdman and Morris.

Most of the patients are young adults, and their general health and over-all reserve are in keeping with their years or are easily restored with multiple whole blood transfusions. The remarkable development of the present blood bank system is one of the factors that make a direct surgical attack on the disease practicable at this time. Abnormal nutritional states from hyperirritability of the intestinal tract and the varying degrees of anemia from direct blood loss in each instance respond to specific therapy. The use o vitamin C, whole blood and non-absorbable sulfonamides permits preparation of the patient for operaf tion

The end to end anastomosis between the terminal portion of the ileum and the distal 3 cm. of the sigmoid over a rubber tube (as popularized by Balfour) reduces the number of suture lines to a minimum, provides adequate decompression proximal to the suture line, thus removing intraluminary tension, and accelerates the rate of wound healing by its "splinting effect," a mechanical factor. The anastomosis should be carried out prior to the surgical removal of the colon.

Six cases from two families are fully described with the operative technique outlined with roentgenographic and photographic studies of the colon reproduced.—*E. G. McDonald, M.D.*

Dye, W. S., Olander, G. A., Monroe, C. W., and Olwin, J. H. Familial polyposis of the colon. *Arch. Surg.*, June, 1951, *62*, 823–832.

The case histories of 11 patients surgically treated for familial polyposis of the colon are presented. All the patients were men and ranged in age from twenty-one to forty-three, the average age being twenty-nine. One patient was a Negro, and the others were white. A familial history of the disease was present in 6 instances and questionable in the seventh. Polyposis was present throughout the entire colon in all cases. Carcinoma was present at the time of operation in 5 cases, and in 3 of the cases there were multiple sites. The sigmoid colon and the rectum were the site of cancer in 4 cases.

Total colectomy was carried out in 6 cases. In 5 cases subtotal colectomy with ileosigmoidostomy and fulguration of the lower segment was done. One patient died of metastatic carcinoma ten months after surgical treatment. One other has clinical evidence of metastasis nineteen months after operation. Nine patients are apparently free of disease.

The cases are presented with the idea of adding to the sum total of cases in the literature in order that over a period of time proper evaluation may be made of the present types of treatment used for this important though relatively rare disease.—*E. G. McDonald, M.D.*

Cassel, Chester, Ruffin, Julian M., Reeves, Robert J., and Stoddard, Leland D. Late effects of thorium dioxide in man. *Arch. Int. Med.*, July, 1951, *88*, 42–50.

Three cases which had received 75 cc. of thorotrast were studied seventeen, sixteen and thirteen years, respectively, after its administration. The persistence of thorium dioxide was shown by roentgen opacity of the liver and spleen, the demonstration of gamma radiation over the organs and the presence of material morphologically compatible with thorium dioxide in liver tissue obtained by needle biopsy. No significant effect was noted on hemopoiesis, hepatic function or the general health of the patients. Clumps of phagocytes containing the granular material, largely in portal fields, were noted and 2 patients had changes characteristic of Laennec's cirrhosis. However, even though the possibility exists, there was no evidence that there was any pathogenetic relationship of the thorium dioxide to the development of the cirrhosis. There were no inflammatory, degenerative, or neoplastic alterations due to the presence of the thorium dioxide.

Although there is no evidence that the thorium dioxide is harmful, the potential dangers of using material with protracted radioacivity which is permanently retained in the body are not disproved by this study.—*Norman Heilbrun, M.D.*

Keil, Philip G., and Landis, S. N. Peritoneoscopic cholangiography. *Arch. Int. Med.*, July, 1951, *88*, 36–41.

The authors describe a technique for direct gallbladder visualization during peritoneoscopy. Fifteen to 40 cc. of iodopyracet concentrated solution (70 per cent diodrast solution) containing 5 cc. of 1 per cent procaine hydrochloride solution is injected directly into the gallbladder. Following removal of the peritoneoscope and needle, films are taken immediately and at five and fifteen minutes. A fatty meal is administered and studies made fifteen and thirty minutes later.

The method is valuable when oral and intravenous methods fail and is the only means of visualizing the ducts except for cholangiography performed during laparotomy. It can be used when the patient's condition contraindicates exploration.

When properly performed the gallbladder, cystic duct and common ducts can be visualized in their entirety. Thus, the method is of value in distinguishing primary hepatocellular disease from secondary hepatic damage due to common duct stone.

Bile peritonitis and other complications have not been observed. The patient with common duct stone may be spared the delay which leads to severe hepatic damage.—*Norman Heilbrun, M.D.*

Rains, A. J. H. Congenital absence of the gallbladder; cholangiography; gall-stone solvents. *Brit. J. Surg.*, July, 1951, *39*, 37–39.

This paper is a brief report on the congenital absence of the gallbladder employing the use of cholangiography for substantiating the diagnosis and the treatment of hepatic duct and common duct stones with ether as a gallstone solvent. A brief discussion on the embryology of congenital absence of the gallbladder is also presented. Seventy-one previous cases have been reported in the literature to 1948.—*Moris Horwitz, M.D.*

## Gynecology and Obstetrics

Müller, C. Ueber die Bedeutung des Druckes bei der Hysterosalpingographie (HSG) und über ein neues Instrument zur Druckmessung. (The importance of pressure in hysterosalpingography and the introduction of a new manometer.) *Schweiz. med. Wchnschr.*, July 7, 1951, *81*, 639–641.

The dangers of hysterosalpingography are listed as follows: introduction or reactivation of infections; mobilization of cells in incipient neoplastic conditions; subsequent tubal pregnancy; sterility because of closure of tubes by oily contrast substances; extravasation of oil into the soft tissues; perforation of the uterus by the cannula; injury of tubal walls. Most of the complications are due to excessive, uncontrolled pressure.

The author has devised a new manometer, which may be sterilized. He shuns fluoroscopic control and recommends a slow instillation of the contrast medium, a water-soluble iodine compound. The pressure should not exceed 150–200 mm. Hg.—*Joseph Zausner, M.D.*

Weiss, R. Lufteinblasung in den schwangeren Uterus bei der Nachfüllung eines Pneumoperitoneums. (Air injection into a pregnant uterus following the refilling of a pneumoperitoneum.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, July, 1951, *75*, 79–83.

The accidental injection of air into a pregnant uterus instead of into the peritoneal cavity is described. The non-suspected pregnancy was of four to five months' duration. The uterus was enlarged to the size of a six to seven months pregnancy by the sudden air injection without inducing uterine contractions or interrupting the pregnancy. Other theoretical dangers could be circulatory disturbance of the placenta induced by the sudden change in size of the uterus, air embolism by way of the uterine vein and bleeding into the uterine cavity from a punctured vessel. None of these complications took place. The intrauterine air disappeared completely in three weeks. A healthy child was born after a normal course of the pregnancy.—*H. W. Hefke, M.D.*

Nieburgs, H. E. Endocrine factors in cancer of the cervix uteri. *Am. J. Obst. & Gynec.*, July, 1951, *62*, 93–101.

Normal growth of cervical epithelium depends on a normal pituitary ovarian-adrenal cortical interrelationship. It is postulated by the author that the continuous stimulating effect of estrogen uninterrupted by progestogen exerts excessive stimulation to the cervical epithelium. Also, a primary decrease in the estrogenic level is usually associated with increased pituitary activity, and the author suggests that this, too, may be responsible for changes in the cervix leading to cancer.

The number of preinvasive cancer cases, if considered in relation to the number of women screened, is equal at all ages and therefore is presumably not related to the menopausal endocrine changes. Excessive stimulation due to estrogens during pregnancy is unlikely since about 99 per cent of estrogens are in conjugated form which is physiologically inactive. There is a large incidence of cancer in nulliparas and women with one child and there is an interval often to fourteen years between pregnancy and cancer in premenopausal women and twenty-five years in postmenopausal women.

These data and several experimental findings are quoted to indicate the association of cervical cancer with conditions responsible for or associated with protracted low estrogenic levels.—*Martha E. Mottram, M.D.*

Fischer, F. K., and Meyer, Lorentz. Joduron-S, ein neues wasserlösliches viskös Kontrastmittel zur Hysterosalpingographie. (Ioduron-S, a new water-soluble viscid contrast medium for hysterosalpingography.) *Schweiz. med. Wchnschr.*, June 16, 1951, *81*, 573–581.

Ioduron-S is a diethanolamine salt of di-iodopyridon-N-acetic acid to which is added a sodium salt of carboxymethyl-cellulose, 1.5 per cent wt./vol. Because of the hypertonic salt content, 1 per cent nupercaine is added for its anesthetic effect. This substance is incompatible with medication containing Ca-Ba-Mg as well as Fe-Cu-Ag-Al ions. Its advantage lies in its rapid absorption. Good contrast is maintained for about fifteen minutes. After one hour, the substance is demonstrable in the urinary bladder. Under pathological conditions, the contrast medium was visible in the pelvis for two hours. The authors use the same material for bronchography and cholangiography.—*Joseph Zausner, M.D.*

Kaltreider, D. Frank. The transverse diameter of the inlet. *Am. J. Obst. & Gynec.*, July, 1951, *62*, 163–166.

The author did 1,167 roentgen pelvimetries by the isometric technique and found:

1. If the obstetrical conjugate is above border line (10.0 cm.) and the transverse diameter is above border line (12.0 cm.), there will be inlet difficulty in only 1 in 300 patients.

2. If either one of these diameters is above border line and the other is below border line, there will be difficulty in 1 of 9 patients.

3. If both the obstetrical conjugate and transverse diameters are below border line, inlet difficulty will be experienced in 1 of 3 patients.—*Martha E. Mottram, M.D.*

MacRae, D. J. Chorionepithelioma occurring during pregnancy. *J. Obst. & Gynaec. Brit. Emp.*, June, 1951, *58*, 373–380.

McRae reviews several aspects of chorionepithelioma occurring during pregnancy with special emphasis on pathogenesis. He suggests a classification of (a) localized chorioma; (b) generalized chorioma. One case of his own is described in which the tumor first showed its presence by bleeding from secondary vaginal metastases, which co-existed with a pregnancy of thirty-three weeks. The vaginal biopsy revealed the typical chorionepithelioma. The Aschheim-Zondek test was positive at dilutions up to 1 in 1,000. Multiple pulmonary metastases were seen in the chest film. Although a live, healthy fetus was obtained by cesarean hysterectomy, the patient died of heart failure on the seventh postoperative day. Autopsy confirmed the hematogenous vaginal and pulmonary metastases. The primary growth was in the center of a bipartite placenta.

The author states that the great variety of chorionepitheliomatous tumors developing in the placenta may be due to the fact that the trophoblastic elements which become malignant are those detached from the placenta and situated deep in the uterine muscle. In this case, however, it is impossible to determine whether the primary malignant cells originated deep in the uterus from desquamated villous elements or whether it was entirely of fetal origin arising in the placenta. Dissemination to the vagina and lungs is characteristic of this tumor. Occasional regression and disappearance of chorionepitheliomatous secondary growths after removal of the primary growth concomitant with progressive lowering of the urinary gonadotropins has been reported.

Although chorionepithelioma with metastases has been considered a fatal disease, recent series indicate recovery can be hoped for in 20 to 30 per cent of cases. This malignancy should be treated by total hysterectomy and bilateral salpingo-oophorectomy with, if possible, postoperative irradiation of secondary deposits.—*Kenneth Kaess, M.D.*

## Genitourinary System

Baena, Figueiredo, and Mattoso Filho, J. Diagnóstico radiológico em Urologia. (A propósito do enfisema retro-peritoneal). (Roentgen diagnosis in urology; retroperitoneal emphysema.) *Rev. brasil. de cir.*, May, 1951, *21*, 371–392.

The authors give an excellent historical review of the various roentgenologic methods of examination in urology to arrive at their main topic which is that of retroperitoneal emphysema.

They state that the perirenal air insufflation introduced in 1921 simultaneously by Rosenstein in Germany and by Carelli and Sardelli in Argentina, although a very useful diagnostic method, failed to gain general applicability owing to the not infrequent fatal accidents which were reported by several nvestigators.

Ruiz Rivas in 1948 proposed a simpler and much safer method, which Mosca and Alvarez named retroperitoneal emphysema and Juri called pararenal pneumography. In this method, the air or gas is injected via the sacral route. The patient is placed on a roentgenographic table in the knee-chest position and a single puncture is made at the level of the sacrococcygeal articulation, 1 cm. either to the left or to the right. A spinal puncture needle is used which, after penetrating the skin, is directed slightly forward and mesially and introduced for about 6 to 8 cm. At this point its position is verified by injecting about 2 cm. of saline solution and re-aspirating to make certain that the needle has not entered a blood vessel. A countertest is made by injecting with the same syringe a small quantity of air. The patient is then placed in ventral decubitus, the needle attached by means of a rubber or plastic tube to an oxygen

tank supplied with a manometer and 500 to 1,000 cc. of gas injected. Following fluoroscopic control of the distribution of the gas, the needle is withdrawn, the patient turned on his back and the first roentgenograms made. In some cases, both kidneys and adrenals are already outlined on these films, in others only one side is visualized, and in still others additional roentgenograms are necessary two or three hours later to obtain the best visualization. The oxygen which is injected in the presacral connective tissue slowly diffuses upward, rendering the retroperitoneal tissues emphysematous and thus producing good contrast for the demonstration of the organs contained therein. The discomfort to the patient is slight and no untoward reactions or incidents are observed.

The authors successfully used the method in 12 cases. The respective roentgenograms are reproduced to illustrate the benefits which may accrue from its introduction as a routine procedure, particularly when combined with other contrast methods of urologic investigation.—*T. Leucutia, M.D.*

VERMOOTEN, VINCENT. Congenital cystic dilatation of the renal collecting tubules; a new disease entity. *Yale J. Biol. & Med.*, June, 1951, *23*, 450–453.

The author has reviewed approximately 700 complete urographic studies consisting of approximately 236 retrograde pyelograms and 464 excretory urograms and believes that he can demonstrate the collecting tubules in approximately 5 per cent of the cases. The fact that visualization of the collecting tubules is possible in only a small percentage of instances indicates that these tubules are dilated and that the opaque medium is collected in them and stasis of the contrast medium in these collecting tubules accounts for the visualization.

The author describes the minimal manifestation of this condition as a thin-veiled filling of a minor calyx with a soft brush-like end. When the collecting tubules are more dilated, one can see a fan-like projection extending out from the minor calyx. Frequently, one can see fine lines radiating out into the kidney, and often they are "beaded," suggesting the presence of multiple, small, cystic dilatations. These fan-like areas of radiopacity vary in intensity and extent. Most commonly they are bilateral and not infrequently they involve all of the renal pyramids, indicating that this is a generalized process involving most, if not all, of the collecting tubules.

The author also feels that the dilatation of the collecting tubules with stasis in these collecting tubules favors the formation of stones and ultimately will give the picture of nephrocalcinosis.

He describes a patient with congenitally dilated cystic collecting tubules who eight years later showed multiple small calculi forming within the dilated tubules. The author is of the opinion that congenital dilatation of the collecting tubules is the end result of damage done to the collecting tubules by the deposition of uric acid crystals in these tubules during fetal life, the faint, fan-like visualization of the collectings tubules being the minimal lesion. Calyceal diverticula appear to be localized lesions of this type, while nephrocalcinosis actually consists of multiple tubule calculi which have formed in these congenitally dilated collecting tubules irrespective of the cause of the hypercalcinuria.—*K. K. Latteier, M.D.*

POWELL, T., SHACKMAN, RALPH, and JOHNSON, H. DAINTREE. Multilocular cysts of the kidney. *Brit. J. Urol.*, June, 1951, *23*, 142–152.

The distinction between single or multiple solitary cysts, polycystic disease, and true multilocular cysts of the kidney has not been clearly defined. The study of the literature and of the 2 cases presented by the authors leads them to suggest that the following criteria should be fulfilled before the condition is accepted as a multilocular cyst: it should be unilateral; it should be solitary; it should be multilocular; the cyst should not communicate with the renal pelvis; the loculi should not communicate with one another; there should be a definite epithelial lining to the loculi; there should be no renal elements within the main cyst; and if residual kidney tissue is present it should be normal.

Multilocular cysts can present at any time from infancy to middle life, but are most common in the third and fourth decades.

The commonest presentation is a palpable mass, but pain and hematuria have also brought patients to the hospital. The condition has been discovered as an incidental finding at postmortem examination.

The lack of communication between the cyst and the renal pelvis probably accounts for the absence of urological symptoms in the majority of cases.

A palpable mass in the abdomen during the course of examination for other purposes first brought attention to the condition in the 2 cases reported.

In one case no soft tissue shadow was visible on the roentgenograms of the abdomen. The excretory pyelogram showed both kidneys to be normally situated, with a slight hydronephrosis of the uninvolved kidney, apparently incident to pregnancy.

The other case showed a rounded soft tissue shadow which depressed the left half of the transverse colon and the splenic flexure. The excretory urogram showed slight elongation of the major calyces with some distention of the upper one.

Nephrectomy has been the usual method of treatment, but resection of the cyst with reconstruction of the kidney has been successful in 2 cases previously reported and in 1 of the cases reported by the authors.

Multilocular cysts differ from solitary unilocular cysts of the kidney only by the presence of intracystic septa. It has been stated that multilocular cysts originate from proliferating tubules which have become separated from and surrounded by normal

renal tissue and that such tubules either become cystic early in life, as a result of continued secretion, or remain dormant for several years.

The authors are of the opinion that the number of loculi in a multilocular cyst corresponds exactly with the original number of sequestrated tubules, and that the chief factor in development is distention and also that the primary group of sequestrated tubules is a Cohnheim rest.—*K. K. Latteier, M.D.*

Levy, S. I., and Hudson, Noble. A case of spontaneous circumrenal haematoma. *Brit. J. Urol.*, June, 1951, *23*, 168–170.

Circumrenal hematoma has been observed in association with a wide variety of renal and suprarenal lesions, and ir association with blood dyscrasias. In some of the cases where a suprarenal growth has been blamed, the authors suspect that the underlying lesion has been a hypernephroma. In a number of cases the cause of the hemorrhage remains unknown.

Spontaneous circumrenal hematoma has been met with more frequently in males than in females. It generally occurs on the left side. It is rarely bilateral.

Classical features of pain, a renal tumor, and signs of internal hemorrhage have been described.

With conservative treatment recovery has been a rare event. Treatment should be operative, and in most instances nephrectomy is indicated.

The authors describe a case of acute circumrenal hematoma occurring in a forty-four year old woman who was suddenly seized with a severe left loin pain and collapsed. The pain suggested a left renal lesion, and a mass was palpable in the left loin. The urine showed no abnormality. Intravenous pyelography revealed slight impairment in function of the left kidney, displacement of the ureter toward the midline and a large left renal outline. In addition to the left renal mass, the patient developed a left-sided pleural effusion which on aspiration proved to be blood stained. Barium meal examination revealed no lesion in the gastrointestinal tract but served to demonstrate that the colon was displaced downward and laterally by a large renal mass.

Seventeen days after the onset of symptoms, the left renal area was explored through an oblique incision. A huge circumrenal hematoma was evacuated and a left nephrectomy was performed. Macroscopic and microscopic examination of the kidney failed to reveal any definite cause for the hemorrhage.

The left pleural effusion was gradually absorbed and convalescence was uneventful.—*K. K. Latteier, M.D.*

Frei, A. Zur Röntgenkontrastdarstellung und Beurteilung von Blasendivertikeln. (Concerning roentgen contrast demonstration and evaluation of diverticula of the bladder.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, July, 1951, *75*, 83–88.

Fifty cases of bladder diverticula are reported, only 1 of which occurred in a female. While their diagnosis can usually be made by cystoscopy, not all of them can be demonstrated; even with surgical exposure, they may be overlooked. The roentgen method by means of air or iodine containing contrast material is the most efficient diagnostic procedure.

The author's technique is to introduce 20 cc. of uroselectan or abrodil into the bladder by catheter. After fluoroscopic observation a roentgenogram is made. Then air is injected until the patient feels pressure. This is followed by further fluoroscopy, which, in the author's opinion, gives the most valuable information. Fluoroscopic observation during micturition often shows what is called "urination into the diverticulum," that is the urine is pushed into the diverticulum instead of into the urethra. After the pressure from micturition stops, contrast material distributes itself again equally between bladder and diverticulum. These findings explain well the bladder residue in cases of diverticula after the obstruction in the bladder neck has been relieved.

Complications by this method were not observed, but the author warns against air injection in cases of bladder tumors, because of the possibility of air embolism.—*H. W. Hefke, M.D.*

Stewart, R. Leslie, and Ross, James A. Congenital recto-urinary fistula. *Brit. J. Urol.*, June, 1951, *23*, 129–138.

Anorectal malformations have been classified into four groups: (1) stenosis of the anus; (2) membranous obstruction of the anus; (3) imperforate anus, but with separation of the rectum from the anus; (4) anus and anal canal normal, but separation of the rectum from the anal pouch. Associated with these anomalies, fistulae connecting the rectum with the bladder, urethra, vagina, fossa navicularis or the perineum occur in approximately 50 per cent of cases.

The greatest number of anorectal anomalies pertain to Group (3), where there is no anal development and the rectal pouch ends blindly some distance above the perineum. The authors present a case report of a recto-urethral fistula associated with this type of anomaly. In the case presented there was no trace of an anus in the perineum and the lower end of the rectum communicated with the urinary tract in the prostatic urethra. This is the most frequent form of developmental fistulous communication between the rectum and the urinary tract. The embryological explanation for this malformation is admitted to still be obscure. The case presented shows the difficulty in determining the exact anatomy of the congenital error in such cases. It is of interest to note that urological examinations undertaken during the early years of life fail to reveal the exact condition. On the other hand, when the patient was fully grown, not only was full investigation facilitated but a clear indication for a simple operative procedure was es-

tablished. The operation proved functionally satisfactory and has afforded complete symptomatic relief.

The initial roentgenograms obtained by injection through a catheter were rather misleading: the cavity was outlined by the contrast medium which could easily be mistaken for a somewhat distorted urinary bladder elongated by its direct communication with the left inguinal colostomy anchored to the abdominal wall. Thus the diagnosis of a rectovesical fistula could be made, especially as urine escaped so freely through the colostomy opening when the bladder was full.

Actually the cystoscopic view of the interior of the bladder, together with the subsequent roentgenograms, showed that the elongated cavity was in reality the lower end of the rectum communicating with the prostatic urethra, while the bladder, of normal shape and capacity, lay in front. The condition was best demonstrated when both the cavity and the urinary bladder were distended with contrast medium.

From these investigations, it was established that the bladder and upper urinary tract were normal but that there was a quite free fistulous communication between the extremity of the lower colostomy loop representing the imperfectly developed rectum and the urinary tract above the external sphincter. In view of the free character of the communicating channel, a simple operative procedure was planned in order to alleviate the leakage of urine from the colostomy.—*K. K. Latteier, M.D.*

## NERVOUS SYSTEM

PENDER, JOHN W., and PUGH, DAVID G. Diagnostic and therapeutic nerve blocks; necessity for roentgenograms. *J.A.M.A.*, June 30, 1951, *146*, 798–801.

The use of roentgenograms in performing diagnostic and therapeutic nerve blocks aids in accurate placement of the needles and furnishes an objective record of the exact position of the needles at the time of injection.

In diagnostic nerve blocks in which the usefulness of the procedure depends upon accurate and selective nerve blocking, the importance of accurate placement of the needle is evident. Without the use of roentgenograms, the position of the needle can be determined only by the relationship of its visible portion and the palpable deeper bony landmarks. Surface landmarks in patients with normal anatomic structure are too indefinite for the accurate localization which is required and are grossly inaccurate when anatomic abnormalities are present. Careful diagnostic nerve block is important in instances where more permanent interruption is desired by section of a specific nerve.

The recording of the exact position of the needle on the roentgen film at the time of a successful nerve block simplifies a repetition of the procedure. Furthermore the injection may be performed at a future time by another person with the same expected results provided a roentgenogram taken before the injection shows the needle to be placed exactly as on the original film.

Anteroposterior and lateral roentgenographic views are used whenever possible. Stereoscopic views may be necessary if a satisfactory lateral projection cannot be obtained. In some cases a lead marker is placed upon a superficial landmark and a survey film is taken to visualize the relationship between the position of the lead marker and the nerve to be blocked. If a needle is inserted and its position is unsatisfactory, the needle should be left in place as a guide and another needle appropriately marked with a lead marker should be introduced until the tip of the needle is observed to be in proper position.—*Gerald Lavner, M.D.*

## SKELETAL SYSTEM

SCHNEIDER, RICHARD C. A syndrome in acute cervical spine injuries for which early operation is indicated. *J. Neurosurg.*, July, 1951, *8*, 360–367.

In acute cervical spine injuries an immediate complete paralysis with hypesthesia at the level of the lesion and an associated sparring of touch and some vibration sense is a syndrome for which early operative intervention is indicated. This opinion is based upon experience with 2 cases which are presented. In both a diagnosis of acute extruded nucleus pulposus was made preoperatively and the lesion confirmed at operation.

The author believes that in the past in cervical cord injuries attention has been paid to the spine and cord but there has been relatively little emphasis placed on acutely herniated discs or on taut dentate ligaments. These latter two factors may play an important part in the production of symptoms and the ultimate prognosis in certain cases. It is stated that following injury marked edema of the cord anteriorly from the recoil of a rebound disc apparently can cause sufficient anterior compression of the cord for the development of the syndrome described above. Under these circumstances, even though no anatomical extrusion of disc material is present, immediate decompression by laminectomy, incising the dura and sectioning the dentate ligaments bilaterally, may relieve the pressure. If actual extrusion of disc material has occurred and operation is delayed, the abnormal portion of the disc may become calcified so that its later removal is impossible.—*R. P. Barden, M.D.*

HUDACK, STEPHEN S. Restitutive approach to lesions of bone. *Cancer*, July, 1951, *4*, 823–834.

The 5 cases described in this paper are excellent examples of the surprisingly good results that may be

obtained by partial resection of the ends of weight bearing bones involved by tumors of low malignancy. The proximal end of the femur was the site of chondrosarcoma in 3 cases, giant cell tumor was present in the proximal end of the tibia in the fourth, and the fifth case was that of a chondrosarcoma of the proximal end of the humerus.

Roentgen diagnosis is mentioned in only 1 case, in one of the lesions of the femur.

The affected portions of the femur and of the humerus were resected and a metal rod prosthetic device placed in the medullary canal of the distal segment of the bone in question. In 3 instances (2 femurs and 1 humerus) this internal prosthesis has been satisfactory enough to permit a nearly normal range of motion in the hip and shoulder joints. In 1 case of tumor of the femur, the chondrosarcoma recurred locally and led to the death of the patient.

The giant cell tumor of the tibia was treated by curettage and not packed with dressings or bone chips. Clearing of infection locally led to excellent healing and function in spite of the fact that the entire tumor was not resected.

The longest postoperative follow-up on these cases is four years.—*I. R. Berger, M.D.*

Garber, C. Zent. Reactive bone formation in Ewing's sarcoma. *Cancer*, July, 1951, *4*, 839–845.

The author presents this case to emphasize the fact that the sun-ray pattern of new bone formation is sometimes found in Ewing's sarcoma of bone. Reactive bone is formed by normal or metaplastically developed osteoblasts in response to various chemical and physical stimuli and has a basic microscopic appearance ranging from immature bone of normal repair to normal, fully developed bone. Its most common examples are found in osteomyelitis and exostoses of bunions. When reactive bone is formed in association with metastatic bone tumors and with Ewing's sarcoma, it complicates their pathological picture.

The case presented is that of a twenty year old woman who had pain and swelling in the thigh for five months prior to thigh amputation. Roentgenograms showed a destructive lesion of the mid-femoral shaft with soft tissue mass and sun-ray effect of bony spicules projecting outward from the femoral shaft. The amputated specimen showed lamination and thickening of the cortex at the site of tumor and radiating bone spicules. A gross pathological diagnosis of osteogenic sarcoma was made; microscopic study conclusively showed the extracortical bone to be reactive bone arising by metaplasia of connective tissue. Scattered between these osseous and osteoid trabeculae were nests of Ewing's sarcoma cells. The patient subsequently died with pulmonary metastases.

In discussing the case, the author indicates that the bony spicules in Ewing's sarcoma are thinner and more hair like than those usually found in osteogenic sarcoma. About 10 per cent of 151 cases of Ewing's sarcoma present this type of bone change.—*I. R. Berger, M.D.*

Nowell, Stanley, Evans, P. R. C., and Kurrein, F. Multiple spontaneous "pseudo-fractures" of bone (Milkman's syndrome). *Brit. M. J.*, July 14, 1951, *2*, 91–94.

This article completely covers the literature since Parkes' first report of a pseudo-fracture of bone in 1882. The papers of Albright *et al.*, considering the syndrome to be a manifestation of osteomalacia (or its juvenile equivalent, rickets) and curable following vitamin D therapy, are discussed in detail.

The authors recommend a survey study of other bones to differentiate from fatigue fracture, the increment fracture of Paget's disease, and other bone diseases, and cough fracture of ribs.

Five roentgenograms are reproduced and 20 references, mostly from foreign literature, are included.

The authors present 3 cases, with pain as the main symptom. All are examples of Albright's group A 2, *i.e.*, raised resistance to vitamin D (R.R.D.). They responded well to calcium and vitamin D therapy; one patient, however, died from massive fibrosis of the liver following infective hepatitis.—*A. F. Rossitto, M.D.*

Durbin, F. C. The early changes of Kienböck's disease of the carpal lunate bone. *Proc. Roy. Soc. Med.*, June, 1951, *44*, 482–488.

In 1910 Kienböck published the first description of the symptomatology and roentgenological appearance of the disease which bears his name.

The condition is one affecting chiefly the right or working hand of young adult manual workers. It progresses through 3 stages:

1. The onset, often following a slight injury, resembles a sprain in that there is a slight pain lasting a few weeks.

2. A period free from symptoms lasts a few months (additional injury may cause the abnormality to be discovered at this time).

3. A period of active disease with symptoms continuing for years terminates in marked osteoarthritis of the wrist joint.

The etiology of this relatively rare disease has given rise to much speculation. The disease is seldom recognized at the onset. The fact that the lunate bone is almost the only bone of the wrist affected suggests an explanation based upon its peculiar anatomy. The lunate bone has the greater part of its surface covered by articular cartilage. There are only two small areas on the anterior and posterior surfaces which have a periosteal covering through which blood vessels can enter the interior. The main blood supply is through the anterior carpal ligament. The posterior blood supply is said to be less efficient. This concentration of the blood supply renders the lunate more vulnerable to trauma. The posterior supply

may be capable of enlarging to take care of the needs of the bone when the anterior supply is damaged or destroyed.

The variation in the relative lengths of the lower end of the radius and ulna is another anatomical feature which may be of importance in Kienböck's disease. Normally the lower ends of the ulna and radius are of equal length. Sometimes, however, the ulna is shorter than the radius (minus variant) and in others it is longer (plus variant). About 40 per cent of wrists have a plus or minus variant. Many authors have noted a minus variant in association with Kienböck's disease, a status which may facilitate trauma by impingement of the lunate bone on the corner of the radius.

There are four main schools of thought concerning the etiology of Kienböck's disease. Three of them regard trauma as the primary cause. The fourth assumes that, in view of a frequent lack of trauma, complete necrosis of the bone takes place as the result of embolic occlusion of vessels, the origin of the embolus not being explained.

Three case histories of Kienböck's disease are presented in detail.

The author believes, from his own experience, that Kienböck's disease is the result of trauma which cuts off the blood supply to the lunate bone and produces avascular necrosis with all its sequelae.

Plaster immobilization, if carried out early, results in restitution of normal bone texture. The immobilization must be continued for a minimum of six months until revascularization has occurred or the roentgen appearance remains static. Probably the best known form of treatment for the established case with symptoms is careful excision of the lunate bone.

In the differential diagnosis of sprained wrist, early Kienböck's disease must be considered as well as fractures of the scaphoid. Care should be taken in looking for compression fractures of the lunate, and if symptoms persist six to eight weeks, additional roentgenograms may show the relatively increased density of avascular necrosis, the forerunner of Kienböck's disease.—*D. R. Bernhardt, M.D.*

Blount, Walter P., and Cassidy, Robert H. Fractures of the elbow in children. *J.A.M.A.*, June 23, 1951, *146*, 699–704.

Fractures about the elbow in children are different from those in adults. Bone growth after the fracture is responsible for the difference. This growth is accelerated following a fracture since the fracture tends to increase the blood supply. A fracture through the metaphysis may retard growth, causing shortening and angulation.

In children, fractures should be treated by conservative means whenever possible. Four hundred and fifty-three consecutive fractures were treated and followed; 268 were supracondylar and required no operative procedure; 84 had fractures of the lateral condyle and required open reduction with fixation. Thirty-eight had fractures of the medial epicondyle; those with more than 5 mm. displacement will usually require open reduction. Twenty-one had fractures of the radial neck; the treatment should be conservative since a poor end result will occur if the head is removed or does not unite.

Miscellaneous lesions include fractures of the olecranon and dislocation of the radial head; these may require open reduction. Radial head dislocations should receive immediate attention. Those of three months' duration should be left alone. The head may later require removal.

Complications are frequent in elbow fractures. The most serious complication is Volkmann's ischemia. Where there is threatened circulatory embarrassment, the vascular problem becomes more important than the position of the fragments; prompt heroic measures are indicated.—*V. L. Peterson, M.D.*

Parsons, Herbert, and Norton, William S. The management of diabetic neuropathic joints. *New England J. Med.*, June 21, 1951, *244*, 935–938.

The authors point out that neuropathic joint alterations occur infrequently as a manifestation of diabetic neuritis. They report 2 cases of Charcot joints occurring in diabetic patients in whom the progress of the degenerative process seemed to have been arrested after lumbar sympathectomy.

The first case is that of a thirty-one year old woman who developed diabetes at the age of eighteen. Her diabetes was poorly controlled and in May, 1944, she developed infection of the right fifth toe taking 3 months to heal. In November, 1945, the right fifth toe and the distal portion of the metatarsal were amputated because of chronic ulcer. She developed a painless swelling of the right first toe, ankle and lower leg in April, 1946, and roentgen examination of the foot on May 11 revealed pathologic fracture through the proximal third of the proximal phalanx of the great toe. Periodic check-up roentgenograms showed decreased density in the tarsal bones with progressive destruction of the metatarsals. A right lumbar sympathectomy was performed on October 3, 1946. Re-examination made in June, 1950, revealed that she had been working as a secretary and filing clerk for two years and that she had no symptoms relative to the feet.

The second case is that of a forty-two year old man who developed diabetes in 1934 at the age of thirty-two. He was seen in 1946 and roentgen examination of the right foot showed calcification of the arteries with marked osteoarthritic changes in the joints of the great toe. There was a fracture of the proximal phalanx of the little toe. This destructive process was found to progress on subsequent examinations until there was destruction about the tarsometatarsal joint with extensive swelling of the foot and skin changes. A right lumbar sympathectomy was done on April 22, 1948. Within two months the patient was much improved and in June, 1950, he reported

that he continued with his work as a taxi driver and had had no further ulcers of the feet.

A review of the literature shows that in all there have been only 22 well documented cases of diabetic Charcot joints reported.—*R. D. Moreton, M.D.*

Dennis, Joseph W., and Rosahn, Paul D. The primary reticulo-endothelial granulomas; with report of an atypical case of Letterer-Siwe's disease. *Am. J. Path.*, July–Aug., 1951, *27*, 627–653.

The authors review the literature on the three major reticulo-endothelial granulomas, namely, Christian-Schüller disease, Letterer-Siwe disease, and eosinophilic granuloma of bone.

Clinically they regard Letterer-Siwe disease as one which follows an acute and malignant course and occurs predominantly in infants and children. Sex incidence is equal. The disease may last for periods ranging from weeks to several years. There are no foam cells in the lesions save in occasional cases and usually they are observed in those of extended duration. There is a hemorrhagic tendency. The "Christian-Schüller triad" is rarely seen. Low grade, continuous fever, moderate to severe secondary anemia, and a moderate leukocytosis or leukopenia appear. Lesions occur almost without fail in the spleen, liver, lymph nodes, skeleton, and skin, and occasionally may be found in the lungs, central nervous system, thyroid gland, gastrointestinal tract and other viscera, and in the thymus, an organ rarely involved by systemic disease. There is no response to treatment, and the disease is invariably fatal.

Eosinophilic granuloma of bone has a benign course. The general health of the patient remains good. The lesion occurs predominantly in infants, children, and young adults under twenty years, although cases up to fifty-eight years of age have been seen. The majority of persons affected are males. The duration is brief, though sometimes the process will recur or become chronic. Only rarely are lipoid cells found. Symptoms and signs are meager: some local tenderness, occasional weight loss, variable eosinophilia. Single or multiple bone lesions are present, and visceral extension is noted infrequently. Eosinophilic granulomatous lesions in the intestine have been reported but their relationship to eosinophilic granuloma of bone is doubtful. Lesions may develop and heal rapidly. The healing of bone lesions occasionally is spontaneous but most frequently it follows surgical or roentgen treatment.

Christian-Schüller disease is a chronic process, with insidious onset, and with extreme variation in course, localization, and clinical manifestations. The patient usually is an adult, although many instances in children are known. Either sex may be involved. The disease lasts for many years. Lipoid cells are present at some time during the course of the disease. Clinical findings depend on the tissues involved and are not specific, although exophthalmos and pituitary diabetes from bone lesions are frequent. Despite the fact that the skeleton is the chief system attacked, almost any organ in the body can be affected directly. The mortality is about 70 per cent. In the very young the disease may have a rapidly fatal course.

The histopathologic features of the three reticulo-endothelioses are given The authors point out the findings which are similar as well as those which, when properly interpreted, tend to distinguish the three syndromes. They concur with the view that Christian-Schüller disease, Letterer-Siwe disease and eosinophilic granuloma of bone result from a single fundamental disorder of the reticulo-endothelial system. Many investigators who are partisans of the doctrine of three distinctly different entities, base their position chiefly on the variation of clinical course and prognosis. It is the authors' impression that differences in the distribution and location of lesions, rather than in the fundamental disease process, are the chief determinants of clinical course and prognosis. By accepting the concept of a single pathologic change it becomes possible to explain the great number of atypical cases which do not fall clearly into any one of the three patterns. According to the authors, this concept suggests that extreme variations in clinical course are due in part to alterations in host or organ resistance paralleling the ageing process. They therefore propose that the three syndromes be designated as "primary reticulo-endothelial granuloma."

The case reported by the authors was undiagnosed prior to patient's death. It was that of a young male thirty years of age who died within 2½ years after onset of disease. The organs involved were the lungs, pituitary, hypothalamus, skin, heart, kidney and lymph nodes. There were no bone lesions. The pituitary was invaded directly by the disease process. Roentgenograms of the chest disclosed a cyst-like fibrotic process in both lower lobes. Histopathologically the principal change in the lungs was a widespread, infiltrative cellular proliferation arising from peribronchial and interstitial tissues. The cysts seemed to be formed from a central breakdown of the denser cell masses.

The age, course, and lack of extension to organs such as the liver and spleen appeared to distinguish the process from Letterer-Siwe disease. The absence of gross skeletal involvement tended to rule out eosinophilic granuloma of bone. Despite the lack of skeletal changes, the course, symptomatology, age, and duration suggested the diagnosis of Christian-Schüller disease. However, microscopically the lesions presented no foam cells, the predominant cell being a large mononuclear histiocyte with a vascular basophilic nucleus. Small giant cells and other inflammatory cells were also present as were areas of necrosis and hemorrhage. The lymphoid tissue was reduced.

The authors, after comparing the clinical and pathologic aspects of their case with those of the three syndromes, conclude that the most probable diagnosis is that of an atypical Letterer-Siwe disease.

The case reported includes excellent reproductions of the roentgenographic, gross and microscopic findings of the lungs.—*R. F. Niehaus, M.D.*

Vogt, A. Die Knochenlymphogranulomatose. (Lymphogranulomatosis of bone.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, June, 1951, *74*, 697–706.

Bone manifestations of lymphogranulomatosis are commonly overlooked during life but are found in 15 per cent at autopsy.

The spine is most commonly affected. This is followed in frequency by the sternum, pelvis, femur, ribs, humerus, scapula and clavicle. Involvement of the spine often is accompanied by paralysis. The differential diagnosis may be quite difficult in primary involvement of the bone. However, spreading to the lymph nodes soon occurs so that the diagnosis can usually be made by biopsy.

Metastasis from other tumors, such as Ewing's sarcoma, reticulum cell sarcoma, etc., must be ruled out in the differential diagnosis. The author believes that lymphogranulomatosis of the bone in itself is sufficiently characteristic, at least to suspect its presence.

The involvement of the bone in lymphogranulomatosis is either focal, with sharp demarcation of the border, or more diffusely infiltrating. The latter form occurs commonly in the acute type. The focal, sharply delineated manifestation is observed in patients with a tendency to a more chronic course. The completely osteosclerotic form is found only in the very chronic types. Involvement of the periosteum is also noted only in association with very chronic lesions. Roentgenographically, one may distinguish five forms of lymphogranulomatosis of bone:

1. A diffuse osteolytic form.
2. The form in which the disease manifests itself as a cyst-like rarefaction with marginal sclerosis and bridges of normal bone between the individual lesions.
3. The periosteal form with elevation of the periosteum.
4. The diffuse osteosclerotic form which gives an appearance of ground glass density of the bone.
5. The trabeculated sclerosing form without any distinct demarcation.

These various forms may occur alone, in combination, or successively.—*H. P. Mueller, M.D.*

Turner, Oscar A. Fibrous dysplasia of bone; neurosurgical considerations in two cases. *Yale J. Biol. & Med.*, June, 1951, *23*, 501–504.

Fibrous dysplasia is a disease which may be manifested in a single bone as tumefaction or a solitary cyst in a region involving contiguous bones, or in a diffuse manner in association with endocrine and developmental disturbances.

Neurosurgical consideration becomes necessary when the cranial involvement simulates the changes often seen in association with a meningioma, or when the progress of the disease produces cranial tumefaction or encroaches upon the intracranial structures.

The author presents 2 cases in which cranial tumefaction occurred in fourteen year old girls, a localized cranial enlargement developing slowly but without pain or tenderness, one child complaining primarily of headaches, the other giving a history of diplopia.

In one instance, the roentgenograms disclosed a marked increase in density involving the lower and outer portion of the left frontal bone, the roof of the orbit, and the lateral wall of the orbit, with extension posteriorly to involve the sphenoid ridge. In addition to the increased density and increased thickness of the involved bone, there was also a vague suggestion of destruction but the roentgenograms indicated a proliferative lesion rather than a destructive lesion. A pneumoencephalogram was normal with no evidence of an intracranial lesion.

The other case revealed a bone tumor involving the posterior portion of the right parietal bone. The outer table was irregularly involved, but the inner table showed less definite evidence of involvement. The lesion was of increased density but appeared to be poorly calcified in comparison to the usual bone tumor. The diploic spaces could not be identified in that region of the skull occupied by the tumor.

Involvement of the cranium by the monostotic form of fibrous dysplasia is unusual though it has been reported previously. The disease simulates the changes frequently seen in a meningioma of the sphenoid ridge and often the problem may be one of diagnosis rather than of therapy.

In the monostotic form the local lesion grows slowly or may even remain stationary once it is manifested clinically. It is not associated with the endocrine disturbances or congenital anomalies described by Albright, and the complete removal of the local lesion, when possible, usually gives a satisfactory result. The pathological process appears to be a true dystrophic change in which normal ossification is inhibited or completely prevented. The disturbance is essentially a benign one, although some cases of sarcomatous change developing in areas of fibrous dysplasia have been reported.—*K. K. Latteier, M.D.*

Ashby, D. W., Williams, G. E. O., and Smith, O. E. Bone dystrophy in association with muscular dystrophy (myopathy). *Brit. M. J.* June 30, 1951, *1*, 1486–1488.

Although textbooks describe bone changes in neuromuscular disorders, similar bone changes in primary muscular dystrophy are rarely mentioned.

The authors report a case of bilateral hypoplasia of the scapulae and humeri in a female aged twenty-eight with generalized muscular dystrophy. Familial study was negative. Roentgenograms and photograph of patient are shown.—*A. F. Rossitto, M.D.*

Murray, Ronald O. Melorheostosis associated with congenital arteriovenous aneurysms. *Proc. Roy. Soc. Med.*, June, 1951, *44*, 473–475.

Melorheostosis, first described by Léri (1922), is a hyperostotic condition of unknown origin characterized by variable clinical features and constant roentgenological findings. Approximately 50 cases have been described.

No hereditary or familial tendency has been reported. Males are more commonly affected than females, and the changes are almost invariably confined to the bones of one limb.

The changes may be found during roentgen examination for other reasons because the condition itself is clinically silent. However, pain, stiffness and limitation of movement in the joints of the affected limb, deformity of the bones involved, and affections of the overlying skin may occur. The onset can usually be traced back to the early years of life and tends to be progressive. Many cases have been associated with various congenital lesions including craniostenosis and scleroderma.

Roentgen examination reveals multiple areas of dense and structureless hyperostosis. The deposits may be quite small or may completely affect a long bone, giving the appearance of guttering wax of a candle. The new bone tends to be deposited cortically in the long bones and endosteally in the short bones. The distribution is peculiarly segmented in pattern, but the segments do not correspond with the course of vessels or nerves. Soft tissue deposits of the bony material also occur but the joint margins are not affected.

The case presented is that of a forty-three year old male who sought medical aid for a sore near his left ankle which had recurred periodically for ten years. His left arm was amputated and the shoulder arthrodesed at the age of twelve for arteriovenous aneurysms, some of which persisted in the stump, supraclavicular region and the back. At the age of twenty-three a tuberculous left kidney was removed. As an infant he was observed to crawl with his left leg doubled up underneath him, but he had no trouble until at the age of thirty-one when his left ankle swelled and was strapped with adhesive bandage. Since then an exfoliative dermatitis has always been present in this area.

The patient was able to play football until the age of thirty-five but since then he has found exercise increasingly difficult due to pain and restriction of movement in the left leg. On examination the movements of the hip were found to be limited in all directions except abduction. Extension of the knee was reduced by 8° and flexion to less than 90°. Plantar and dorsiflexion of the ankle were normal but inversion and eversion were not possible. Hard masses were palpated in the adductor region near the left hip joint and considerable deformity of the left tibia was present with overlying skin change.

Roentgenograms revealed typical and widespread changes involving the left limb, with dense patches elsewhere on the left side of the body including the sacroiliac joint, the bodies of C-4 and D-9, the 8th and 9th ribs and the superior and inferior angles of the scapula. The skull was not affected.

It has been reported that the pain and limitation of movement in these cases can be relieved considerably by sympathectomy.—*D. R. Bernhardt, M.D.*

## Blood and Lymph System

Seibert, F. M. Zur Technik der Kontrastdarstellung von Aneurysmen (Methodik der einzeitigen Darstellung von Aneurysmen in 2 Ebenen). (Concerning the technique of contrast visualization of aneurysms; method of simultaneous visualization of aneurysms in two planes.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, June, 1951, *74*, 707–713.

The pathogenesis and classification of traumatic aneurysms are discussed.

The surgeon is helped by demonstration of the aneurysmal sac, its afferent and efferent vessels and the neighboring vessels. Direct injection of the artery with compression of the vessel proximal to the site of injection is preferred to direct injection into the aneurysm. Perabrodil in 50 per cent solution is used as contrast medium and simultaneous exposures in two planes are obtained by the use of the Dyes apparatus usually employed for cerebral angiography.

Two cases are presented, both without and with contrast medium injection.—*F. M. Reis, M.D.*

Scott, H. William, Jr., and Roach, John F. Phlebography of the leg in the erect position. *Ann. Surg.*, July, 1951, *134*, 104–109.

Ordinary methods of phlebography in the horizontal position do not adequately visualize the deep venous system of the leg; also the presence or absence of competent valves in the deep and communicating veins is not usually completely demonstrated in the recumbent position.

A brief review of the literature and history of phlebography is given. The authors' method consists of tilting the roentgenographic table to an angle of 75 degrees from the horizontal. The patient stands on a foot rest with the leg to be studied in the midline of the table. A tourniquet is placed about the leg just above the ankle and tightened sufficiently to obstruct the superficial venous system. After a needle is inserted into a vein on the dorsum of the foot, 20 cc. of diodrast is injected over a period of five to ten seconds, and the first exposure is made. The tube is then shifted and a second exposure is made giving a stereoscopic pair of films. A second injection is not needed because the contrast medium, even in normal indi-

viduals, leaves the venous channels of the legs rather slowly with the patient in the erect position. If the tourniquet at the ankle is applied properly the material is directed entirely into the deep veins of the leg. No contrast material appears in the superficial veins unless the valves are incompetent. The valves that are present are customarily recognized by the fusion dilatations along the course of the veins.

The authors generally feel that it is not necessary to study the entire venous system of the lower extremity from the ankle to the groin, but at present confine their studies to that of the popliteal vein and its tributaries from the lower third of the thigh to the ankle.—*E. L. Pirkey, M.D.*

MOORE, H. D. Deep venous valves in the aetiology of varicose veins. *Lancet*, July 7, 1951, *2*, 7–10.

The author performed venograms on 102 patients with varicose veins by using the following method which particularly visualized the deep veins of the leg. The contrast material ("pyelosil") was injected into any vein of the foot in the supine position. A tourniquet was placed at the ankle and a pneumatic tourniquet around the thigh, the latter to occlude both the venous return and the diastolic inflow of arterial blood.

By this method the valves of the deep veins are well seen, the muscular vessels fill, and any filling of superficial veins must be from deep to superficial as a result of incompetent valves in the communicating veins.

Eighteen of the cases had a history of deep venous thrombosis and 84 did not. None of the 18 and two-thirds of the 84 had no visible valves in the deep veins, as demonstrated on the venograms.

Two-thirds of the thrombotic legs and all of the valveless non-thrombotic legs had similar venograms.

The author concludes that, if the valveless state of the thrombotic legs is the cause of superficial varicose veins, ulceration, and other symptoms, the absence or functionless state of the valves in many non-thrombotic legs must likewise be the cause of varicose veins and their complications in such legs.—*Norman Heilbrun, M.D.*

OLIVIER, CL., and SABATIER, G. Les phlébites anciennes des membres inférieurs propagées à la veine cave inférieure: dangers éloignés de la ligature de ce vaisseau pour maladie thrombo-embolique. (Old phlebitis of the lower extremities with extension to the inferior vena cava; potential danger from ligature of this vessel in thrombo-embolic disease.) *Presse méd.*, July 4, 1951, *59*, 948–952.

The authors review 7 personal cases and survey 29 cases found in the literature. Their studies included venography and demonstrated the length and poor capacity of the compensatory venous circulation particularly in the male.

The conclusion is reached that interruption of the inferior vena cava below the renal veins is not in itself potentially serious. In large part, the danger lies in thrombosis of the iliac veins. Thus, with ligature of the vena cava for an accidental wound the occurrence of an up-stream thrombosis is rare and potential sequelae are mild. On the other hand, in thrombo-embolic disease such a ligature favors the development of a retrograde iliac thrombosis. The difficulty of re-establishing adequate venous return to the heart is emphasized.—*M. L. Sussman, M.D.*

MOSES, CAMPBELL, and PLATT, MADELINE. Changes in the total circulating eosinophile count in cyclotron workers. *Science*, June 15, 1951, *113*, 676.

This report is based upon observation of 3 workers who received an overexposure of radiation while sanding the copper dees of a cyclotron. Routine red and white blood cell counts prior to this exposure failed to reveal any significant variations and only a transient leukopenia was detected after the exposure.

Total circulating eosinophil counts were made after exposure and a marked increase above the normal was apparent in 2 of the 3 exposed workers. The elevated circulating eosinophil counts gradually returned to normal during a period of about ten weeks.

It is suggested that the total circulating eosinophil count may be a useful indicator of exposure to radiation in individuals employed in roentgenologic, cyclotron and other laboratories with radiation hazards.—*W. M. Roy, M.D.*

KEELEY, JOHN L. A bullet embolus to the left femoral artery following a thoracic gunshot wound; probable entrance through thoracic aorta; case report and résumé of peripheral arterial bullet emboli. *J. Thoracic Surg.*, June, 1951, *21*, 608–620.

A case of thoracic bullet wound followed by embolization to the left femoral artery is presented. This appears to be the sixth surviving case of its kind, 5 others having been found in the literature. In addition, 15 other cases in which bullet wounds of the heart or associated great vessels had been followed by peripheral arterial embolization of the foreign body are summarized.

Therefore, in instances of bullet wounds with only a wound of entrance, failure to demonstrate the foreign body in the expected region should prompt the suspicion that it may have entered the cardiovascular system and been carried away, thus suggesting that other parts of the body be studied roentgenographically. Early motor and sensory paralysis due to ischemia may suggest the erroneous diagnosis of a lesion of the nervous system. Finally, the correct diagnosis should lead to early embolectomy, a recommendation made by Schloffer in 1903. With the pres

ent improvements in the technique of embolectomy, recoveries from aortic or cardiac wounds with embolization of the foreign body might, in the future, be complete even to the survival of the involved extremity.—*T. C. Stansbury, Jr., M.D.*

Shimkin, Michael B., Mettier, Stacy R., and Bierman, Howard R. Myelocytic leukemia; an analysis of incidence, distribution and fatality, 1910–1948. *Ann. Int. Med.*, July, 1951, *35*, 194–212.

The authors make a statistical analysis of 212 patients with chronic myelocytic leukemia seen in three San Francisco hospitals in the period of 1910 to 1948. With this are compared the data of nine other similar reports totaling 975 patients, and further compared to the mortality statistics of the United States.

All data show a continually increasing incidence of cases of chronic myelocytic leukemia. This may be explained by better diagnosis, better reporting and better filing of records. Nevertheless, more cases will be seen and recognized by all physicians.

There is a definite shift of increase in the female population. Statistically it is not due to the increasing proportion of females in the living population. A hypothetic reason may be the increasing employment of women in industries where they may be exposed to radiation or benzol.

There has been a progressive increase in the age of onset. This parallels our progressively older living population, rather than a shift toward an older age of onset.

All available data show no significant change in the duration of illness. The mean survival is from three to four years after apparent onset. Twenty per cent of patients live for five years or longer and 2 per cent survive over ten years. The age of onset plays no role in the prognosis as far as longevity is concerned.

No form of therapy is curative and none is known at present to increase the life span. Radiation therapy is purely palliative and the dosage should be the minimum to produce the desired result.

Many interesting and important facts regarding leukemia are at present impossible or extremely difficult to demonstrate because of the limited number of cases seen by even the largest centers. Adequate control series using single therapeutic agents are not available.

There should be a nation-wide systematic plan of study accepted and followed by many institutions with central correlation of the information to evaluate the soundness of therapeutic agents.—*Joseph Levitin, M.D.*

Slentz, William A. Leukemia and pregnancy; report of four cases and review of the literature. *Ann. Int. Med.*, July, 1951, *35*, 59–68.

Four cases are reported with 6 additional cases reviewed, collected from the literature.

The authors conclude that leukemia is not an indication for termination of a pregnancy. In the chronic cases 75 per cent of the babies are normal and there is little logic in sacrificing the life of a baby in the hope of prolonging the life of an already doomed mother. Leukemia is not transmitted to the children and the pregnancy per se does not alter the course of the disease. Delivery is tolerated by the mother as well as any operative procedure and death from uterine hemorrhage is rare. Leukemia may cause premature birth.

There is no available treatment for the acute case. In the chronic cases, treatment other than high voltage roentgen therapy, as Fowler's solution, transfusion is preferred. Roentgen therapy must be cautiously given to avoid injury to the fetus.—*Joseph Levitin, M.D.*

Isaacs, Raphael, and Trimmer, Ralph W. Blood cell changes in leukemia during aminopterin therapy. *Ann. Int. Med.*, July, 1951, *35*, 236–239.

Aminopterin is an antifolic acid substance. Giving aminopterin creates a folic acid deficiency.

A case of chronic myelogenous leukemia in the advanced blast stage was treated with aminopterin. Changes in the peripheral blood and bone marrow characteristic of folic acid deficiency were found. These were macrocytosis, multilobulation of the neutrophils in the peripheral blood; and megaloblasts and giant metamyelocytes in the bone marrow.—*Joseph Levitin, M.D.*

de Silva, C. C., and Weeratunge, C. E. S. Cooley's anaemia in Sinhalese children. *Arch. Dis. Childhood*, June, 1951, *26*, 224–230.

The authors present the first recorded cases of Cooley's anemia in the Sinhalese. They discuss the racial association with the Mediterranean race, through the works of Coon, Shanklin, and Chanmugam. The investigations of Chanmugam and Coon entailed comparative measurements with indices by Chanmugam and the comparison of statures of the Sinhalese with the Mediterranean by Coon. Shanklin found two varieties of the Mediterranean race living in the Transjordan and Syrian deserts who are closely related to the Sinhalese in stature and language.

Four patients are reported. The youngest, three and one-half months of age, had the typical blood picture and a large spleen without any bone changes. Two brothers and one other boy exhibited all the findings of Cooley's anemia both clinically and roentgenologically.

A good discussion of the disease entity is presented with a detailed analysis of the blood picture and roentgen findings showing the mosaic pattern of the bones of the hands and the characteristic "hair standing on end" appearance of the skull.—*L. L. Lemak, M.D.*

## RADIATION THERAPY

Wayte, A. B. Treatment of some disorders of the pituitary by radiotherapy. *Proc. Roy. Soc. Med.*, June, 1951, *44*, 450–452.

Roentgen therapy has been used in the treatment of pituitary disorders for over forty years. In 1907 Gramegna treated a thirty-seven year old woman for acromegaly. The woman responded well but relapsed a year later. A second course was unsuccessful.

Béclère successfully treated a fifteen year old girl in 1908 for acromegaly. The patient was alive and well fourteen years following irradiation.

In spite of these early beginnings, knowledge of the effects of irradiation on the pituitary is incomplete and there is considerable disagreement on suitability, technique and dosage. The rarity of cases, the interplay of pressure and glandular phenomena, lack of histological confirmation and the tendency to spontaneous remission make accurate assessment of the response to treatment difficult.

Sufficient data have been published to permit some tentative conclusions to be drawn. Results appear to be better in most pituitary tumors when a single course of treatment of 3,000 to 3,500 r, measured at the pituitary, is given in an over-all period of three to four weeks. Dosage below 2,000 r is less effective and the safe upper limit is probably over 4,000 r.

The author has found no evidence of cerebral or pituitary necrosis attributable to radiation. Irradiation does not prevent or render more difficult subsequent surgery, should it become necessary. This cannot be said of repeated or protracted courses. Kerr, in 1948, published a series of 50 cases treated with this dosage; 70 per cent of the acidophil and chromophobe cases had good results. The only basophil case did not respond.

For the last four years a technique has been employed at Guy's Hospital planned to give 3,500 r at the pituitary in twenty-eight days, with 200 kv. corresponding to a half-value layer of 1.9 mm. Cu. Five ports of entry, 4 by 4 cm. are used arranged over the frontal and frontotemporal areas, each port receiving a skin dose of about 2,400 r. Treatment is started with 300 r to one field for the first two days; thereafter two fields a day are treated with 250–300 r.

Twenty-three patients have been irradiated with this technique and no untoward symptoms have occurred during treatment. Two patients showed a mild sinusitis about two weeks after treatment which rapidly cleared. Epilation has been minimal, in no case unsightly, and the hair has regrown.

The adult pituitary gland appears to tolerate irradiation well. One patient died four months after treatment. Histological sections of his pituitary gland, which received 3,600 r were reported as normal. Kerr reported 3 patients who died between six months and five years after similar irradiation. No pituitary changes attributable to irradiation were found.

Experimental evidence suggests that overactive elements of the pituitary gland may be relatively more sensitive to irradiation than normally functioning pituitary tissue.

Pituitary lesions are so apt to undergo spontaneous remissions that a follow-up of less than ten years is almost without value.

Four case histories are briefly reported.

Successful treatment of Cushing's syndrome by radon implantation has been reported by Pattison and Swann. Two cases had failed to respond to deep roentgen therapy and were implanted with radon seeds. Retrospective calculation indicates that a dose of at least 15,000 r was given to most of the pituitary area.

The prognosis in basophilism is poor. The life expectancy is usually two to five years, the survival being somewhat shorter in men than in women. In a series of 21 cases 10 were men and 11 women; 9 of the men died within five years as against 2 of the women —*D. R. Bernhardt, M.D.*

Baclesse, F. La roentgentherapie seule dans le traitement des cancers du sein. (Roentgen therapy alone in the treatment of cancer of the breast.) *Radiol. clin.*, Sept., 1950, *19*, 284–293.

The principle of the method developed during the past fifteen years at the Curie Foundation for the roentgen irradiation of mammary carcinoma is based on three factors: (1) chronologic observation of the cutaneous reactions with the aim of avoiding exudative epidermitis and thereby increasing the dose; (2) administration of a large dose through well circumscribed tangential or side-view fields; and (3) very long protraction with daily fractionation extending over a period of three to four months or longer.

A preliminary biopsy is indispensable for establishing a precise diagnosis and evaluating the degree of radiosensitivity of the cancer. Of 241 cases treated by roentgen therapy alone from 1936 to 1948, a biopsy was taken in 166, the relative percentage having increased considerably since 1944. The only lesions in which biopsy is contraindicated are the acute and subacute ones. It is advisable to begin with the irradiation as soon as possible after the biopsy.

The technique of irradiation is as follows: (a) *Factors.* 180–200 kv., 1 mm. Cu, 20 r/min., and a skin target distance of 50–60 cm.

(b) *Fields.* Six to seven fields are used and overlapping is prevented by outlining the margins of the fields with the aid of three suitable landmarks. One of these landmarks corresponds to the middle of the clavicle, the second and most important is at the junction of the mammary gland with the free border of the pectoralis major muscle and the

third lies in the anterior axillary fossa at the elongation of the anterior axillary line. The landmarks are indicated with silver nitrate or better still are tattooed on the patient with india ink after puncture of the skin with a small lancet. The fields are outlined with the patient in the position ready for irradiation (Fig. 1) The mammary fields must be irradiated tangentially, the patient lying on her left or right side with the arm elevated In voluminous breasts an additional direct anterior field is used.

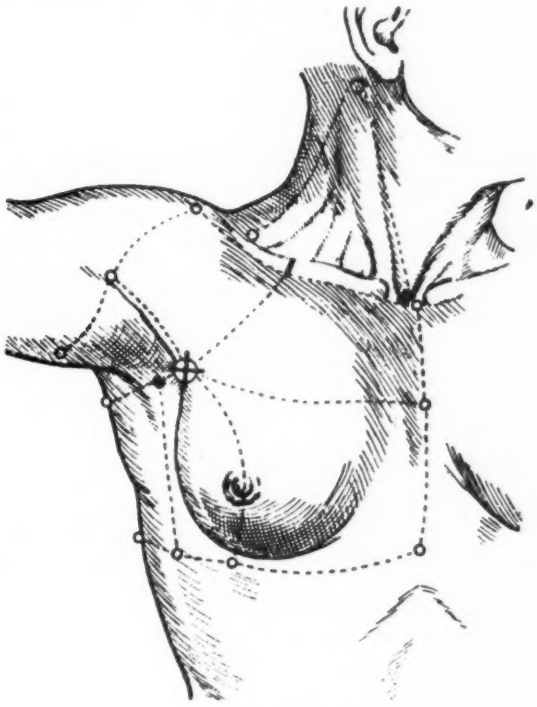

Fig. 1. View of the fields of irradiation with the three cutaneous landmarks used for the treatment of mammary carcinoma by roentgen therapy alone. (Reproduced by permission from Baclesse, F., *Radiol. clin.*, Sept., 1950, *19*, 284–293.)

The size of the fields in the average person is 10 by 10 cm. or 10 by 12 cm., but after the administration of 4,000 r this must be reduced to prevent accidents. The treatment is carried out in a rotating manner by irradiating 2 fields at one time so that every field is exposed twice weekly. The employment of a luminous field localizer is absolutely necessary.

(c) *Dose.* The skin dose on the mammary fields varies between 4,000 and 6,000 r per field. The tumor dose in the center of the breast must be at least 6,000 r but it may have to be as large as 9,000 r to obtain satisfactory results. A cutaneous dose of 4,000 to 5,000 r is required on the axillary field and of 4,500 to 5,200 r on the supraclavicular field.

(d) *Protraction.* In mammary carcinoma of average radiosensitivity the protraction lasts three months, but in the more radioresistant type it may have to be extended over a period of four and even four and a half months.

(e) *Daily Dose.* It is advisable not to exceed a dose of 200 to 250 r per field in one day. Since on an average two fields are irradiated every day the total daily dose is 400 to 500 r.

In evaluating the end results, the author studied statistically a series of 130 patients with mammary carcinoma of Stages II, III, and IV, treated by roentgen therapy alone between 1936 and 1945. Of these, 41 were completely free of carcinoma after five years or longer. In further breaking down these figures, it was noted that the best results were obtained in the small tumors and some of the ulcerated tumors.

The post-irradiation sequelae were tabulated for. 156 cases. These included marked telangiectasis (20 per cent), telangiectasis with sclerosis and edema (17 per cent), sclerosis of the pectoral muscle (9 per cent), moderate swelling of the arm (5 per cent), pulmonary fibrosis (7 per cent), cutaneous necrosis (6 per cent), neuritis (1.5 per cent), rib fracture (0.6 per cent), and paralysis (0.6 per cent).

The changes in the hematologic pattern due to the long protraction were carefully recorded by Lavedan in 89 patients. A decrease in the number of the red corpuscles was present in 49 and of the white corpuscles in 60 cases, whereas 37 patients developed an increase in the number of the red corpuscles, 29 an increase in the number of the white corpuscles and 11 an increase in the number of both.

In concluding, the author stresses the great burden which this method places on the radiotherapist, who needs long experience, as well as on the patient, who must have endurance and patience. The economic aspect must also be taken into consideration.—*T. Leucutia, M.D.*

Richmond, J. Jackson. The importance of radiotherapy in the treatment of ankylosing spondylitis. *Proc. Roy. Soc. Med.*, June, 1951, *44*, 443–447.

Despite the fact that the rheumatic diseases have received increasing attention by the medical profession in recent years, the definite diagnosis of ankylosing spondylitis frequently is not made in less than five years. There is an average lag of three years before the institution of roentgen therapy after the patient has sought medical advice.

This paper is based upon 160 cases of ankylosing spondylitis covering the author's experience in the last seven years.

Sex and incidence: 143 males, 17 females.

Average age at institution of roentgen therapy: 32½ years.

Average time interval between patient seeking medical advice to commencement of irradiation: 3.1 years.

Occupation: heavy manual labor: 19 patients; light

manual labor: 60 patients; sedentary: 32 patients; Armed Services: 43 patients.

Pathology: Knowledge concerning the pathology of ankylosing spondylitis is far from complete. The lesion differs from rheumatoid arthritis in its selection of joints, method of spread and response to therapy. However, they both present features of an infective process. Classically, the sacroiliac, intervertebral, costovertebral and costotransverse joints are involved. The extra-spinal sites of involvement are hips, shoulders, knees, temporomandibular joints, sternoclavicular joints and wrists.

Diagnostic features: (1) spinal stiffness, (2) diminished thoracic expansion, (3) raised blood sedimentation rate, (4) roentgenographic changes in sacroiliac joints.

Methods of roentgen therapy: (1) wide field therapy; (2) periodic conservative therapy with relatively small doses directed to the painful areas; (3) localized semi-intensive therapy in which the irradiation is directed to the sacroiliac joints and lower lumbar spine first; (4) generalized semi-intensive therapy in which the sacroiliacs and entire spine are treated. There are differences of opinion concerning dosage. The author gives a surface dose of 2,000 r to each section of the spine over four weeks using 250 kv. with a half-value layer of 1.9 mm. Cu. The dose is delivered in fractions of 100 r per day to sacroiliacs, lumbar, dorsal and cervical regions for twenty treatment days. To minimize pelvic irradiation in premenstrual women a tangential sacroiliac field is used.

Results: These are shown in the following table:

PERCENTAGE COMPARISON OF RESULTS BETWEEN LOCALIZED AND EXTENSIVE ROENTGEN THERAPY

(1) *Sacroiliac Joints*

| *Immediate Result* | | | *Long-Term Result* | | |
|---|---|---|---|---|---|
| No improvement | Moderate improvement | Good improvement | Excellent improvement | Improvement maintained | Recurrence of symptoms |
| 11% | 33% | 48% | 8% | 47% | 53% |
| (2) *Entire Spine and Sacroiliac Joints* | | | | | |
| 4% | 28% | 51% | 17% | 80% | 20% |

—*D. R. Bernhardt, M.D.*

DeNavasquez, S. J., Trounce, J. R., and Wayte, A. B. Lipoid pneumonia (non-inhalation) in carcinoma of the lung treated by radiotherapy. *Lancet*, June 2, 1951, *1*, 1206–1208.

The authors state that inhalation lipoid pneumonia has been well covered in the literature and with numerous case reports. However, they do not believe that the non-inhalation type has previously been reported.

They cite the case of a fifty-six year old woman with an anaplastic bronchogenic carcinoma of the right upper lobe treated by roentgen therapy. She received a tumor dose of 4,000 roentgens in twenty-eight days through six portals. She improved both clinically and roentgenographically. Approximately twelve weeks after therapy she developed increasing breathlessness and pain in her left chest. Roentgenograms of the chest revealed fairly dense shadows spreading out from both hilar zones to the lung periphery and confined to the mid-lung regions. The areas of densities corresponded to the distribution of the radiation. The patient became worse and died.

On section the macrophages of the lung tissue were loaded with fat. No tumor cells could be detected. The anatomical diagnosis was lipoid pneumonia. The authors believe that the fatty change was due to a degeneration, liberating lipoid which was subsequently phagocytosed by macrophages which accumulated in the alveolar spaces and produced pneumonic consolidation. The pneumonic consolidation was like that seen in lipoid pneumonia due to the inhalation of oil but differed both in the nature of the fat and in its pathogenesis. The authors have to date observed 4 such cases.—*R. A. Hays, M.D.*

Burford, E. Humber, Glenn, Joseph E., and Burford, Cyrus E. Therapy of Peyronie's disease. *Urol. & Cutan. Rev.*, June, 1951, *55*, 337–338.

It is noted that this disease, which is due to a fibrosis of the sheaths of the corpora cavernosa, may occur between the ages of twenty and ninety years, the average age being fifty-three. Trauma has been considered as an etiological factor in the deposition of fibrous tissue in those patients with faulty metabolism. The localization of the fibrous plaques among 124 cases observed by the authors was 64 on the dorsal, 9 on the lateral, and 7 on the ventral aspect of the corpora cavernosa. Five patients had more than one area of fibrosis simultaneously.

The pathologic examination shows a pearl gray, glistening scar-like tissue usually measuring 3 to 5

mm. in thickness and with some nodularity. It resembles keloid formation and frequently contains calcium deposits.

Ninety-one patients had topical application of radium at one or more sittings for an average amount of 120 mg. hr. for a single treatment. More recently the authors have combined radium therapy with tocopherol with improvement in their results.—*G. W. Chamberlin, M.D.*

Tod, Margaret C. The place of x-ray therapy in the treatment of malignant ovarian tumours. *J. Obst. & Gynaec. Brit. Emp.*, June, 1951, *58*, 385–387.

The author outlines two possible methods of roentgen therapy of malignant ovarian tumors. (1) The smallest possible volume of tissues which can be regarded as likely to contain the whole tumor can be irradiated to the highest dose which the local tissues can stand. (2) The whole region likely to be invaded by the tumor and the most probable sites of secondary deposits can be irradiated to the highest dose which systemic tolerance will allow. As it is felt the local tolerance of pelvic tissues is not much greater than that of the whole peritoneal cavity, the second possibility is followed at the Holt Radium Institute.

A special appliance designed to ensure homogeneous irradiation of large volumes is described as well as the treatment technique. Briefly, a total dose of 3,000 roentgens is delivered homogeneously throughout the volume treated in four weeks utilizing four oblique fields usually 20 by 30 cm. The five year crude survival rate of 102 cases completely treated was 37 per cent. Thus, radiation therapy appreciably increased the chance of survival and gave definite beneficial clinical effects.—*Kenneth Kaess, M.D.*

White, William Crawford, and Finn, Frederick Wall. The late complications following irradiation of pelvic viscera. *Am. J. Obst. & Gynec.*, July, 1951, *62*, 65–74.

Many months or years may elapse before the complications of radium or roentgen therapy for carcinoma of the uterus appear. It may be that the routine use of antibiotics and the administration of the roentgen therapy prior to the radium application may reduce the injuries to bowel and bladder.

The following late complications are discussed:

*Bone*: The incidence of fracture is about 1 per cent. The usual site for fracture is the femoral neck and rarely the os pubis. All fractures are preceded by prodromal pain. The fractures may be either complete or incomplete.

*Urinary tract*: The authors cystoscope every patient and do intravenous urography before starting irradiation. Late complications may be ushered in with frequency, hematuria and dysuria, or there may be an insidious onset.

Complications include indolent ulcers of the bladder, vesicovaginal fistula, intramural stricture of ureter and the secondary hydroureteronephrosis.

*Intestinal tract:* Many cases with milder symptoms never see the physician. Aldridge, of the Women's Hospital, states that 17 per cent of women have post-irradiation stricture and Maas, of Wisconsin General Hospital, reports 50 to 75 per cent of patients with permanent residual rectal changes after irradiation.

Proctitis frequently develops early and clears up gradually, but may leave ulceration, scarring and stricture. This process may also occur in the colon above reach of the proctoscope. McIntosh and Hutton prefer palliative therapy for these cases. The authors had 4 deaths in 26 cases given palliative therapy and they feel that these patients should be followed very closely to avoid complete obstruction, perforation or fatal hemorrhage. In those patients on whom they operated electively with adequate preparation they had no deaths.

Strictures may also occur in the ileum. In cervical stump cases a loop of ileum may be adherent to the operative site and thus receive the full radium dose. The authors have had several cervical stump cases with adherent bowel and feel that roentgen studies and even an exploratory celiotomy are indicated prior to radium application. Two cases had injury both to sigmoid and ileum.—*Martha E. Mottram, M.D.*

## RADIOISOTOPES

James, Arthur G., Williams, Roger D., and Morton, Joseph L. Radioactive cobalt as an adjunct to cancer surgery. *Surgery*, July, 1951, *30*, 95–105.

The authors are desirous of supplementing radical cancer surgery with a therapeutic agent similar to but more adaptable than radium. Radioactive cobalt is their choice.

They cite the following advantages of $Co^{60}$:

1. Penetrating beta rays are more easily completely filtered. It is therefore possible to irradiate cancer in proximity to bone.

2. Cobalt lends itself to use in multiple weak sources making possible treatment in previously heavily irradiated areas.

3. Irregular volumes can be more easily implanted because of the flexible nylon applicators.

4. The cost of cobalt is less than that of radium.

5. It is simply calibrated by means of an electroscope.

6. Being a magnetic metal, it can be handled with an electromagnet.

7. It is safer to handle since it does not form gaseous radioactive products on decay and there is no powder to be absorbed in case of breakage.

Radioactive cobalt is cut into 3 mm. lengths for loading within flexible nylon tubing. The wall thickness is such as to filter all but insignificant amounts of beta rays. The loaded applicators may be

implanted into any site which can be reached by long, straight Keith or curved tension needles, or by straight or grooved pointed guides used like aneurysm needles.

During the past year 53 patients were treated. Thirty-eight patients had lesions of the head and neck, 8 of the abdomen, 4 of the chest and 3 of the extremities. Examples are cited illustrating the applications of radioactive cobalt in each of these locations.

The authors state that no conclusions may be drawn at this early date. The method of irradiation appears worthy of further clinical trial.—*F. W. O'Brien, Jr., M.D.*

KELLY, SALLY, and BAILY, NORMAN A. The uptake of radioactive iodine by ascophyllum. *Biol. Bull.*, June, 1951, *100*, 188–190.

Uptake of $I^{131}$ in segments of the brown alga *Ascophyllum nodosum* was measured after exposure for various intervals of up to twenty hours to either labelled artificial sea water or to labelled natural sea water. A constant exchange process was noted between iodine within the algae and iodine in the immersion medium. A graph shows that equilibrium was reached in about two hours.

These observations are unique in that uptake of a tracer element, which is also an anion, is reported.—*Z. S. Gierlach, M.D.*

SCHWAIGER, M., and SCHMEISER, K. Zur Methodik der Blutvolumenbestimmung mit Radiophosphor ($P^{32}$). (Method of determination of blood volume with radioactive phosphorus, $P^{32}$.) *Klin. Wchnschr.*, Aug. 15, 1951, *29*, 536–540.

The authors feel that the current methods of blood volume determination, the CO method and the dye methods, are too complicated and too inaccurate for routine clinical use. They have therefore adopted the method using radioactive phosphorus, $P^{32}$, which was first suggested by Hevesy in 1942. They modified the original method slightly, used it first on animals and then on a large number of normal persons and patients. Clinical results of these studies will be published elsewhere.

The fundamental principles of the method are described in the present paper. Two and a half hours before the beginning of the blood volume determination 15 ml. of blood is withdrawn from the cubital vein and placed into a small sterilized Erlenmeyer flask which contains 0.5 ml. of sterile vetren (heparin). $P^{32}$ of sufficient quantity to result in about 50 microcuries for the material later to be reinjected is added and the mixture is shaken briefly by hand. It is then placed into a mechanical shaker for a period of two hours at a temperature of 37.5°C. After three hours the erythrocytes are practically saturated with $P^{32}$. The blood is then divided into two parts. One part is used to determine the erythrocyte activity and the hematocrit. The other part is injected intravenously into the patient. A given time (usually between 5 and 30 minutes) after the reinjection about 6 ml. of blood is again withdrawn from the vein; 2 ml. is used for the hematocrit and 4 ml. for the final test preparation; 0.2 ml. of vetren is again added to the 4 ml. of blood and the solution is centrifuged for twenty minutes at 2,500 revolutions per minute. Since only the radioactivity of the sediment is of value, the plasma is removed. Saponin solution (1 per cent) is added to produce complete hemolysis and the solution is dried on a watch glass, powderized and definite quantities deposited on aluminum cups for activity measurements with the Geiger counter.

Detailed formulas for the determination of the total erythrocyte volume, the total blood volume, as well as for increasing or decreasing volumes from these measured data are given. Sources of error are discussed. They are of the order of 5 per cent for determination of blood volumes and increasing blood volumes while they vary, of course, widely for decreasing blood volumes.

A permissible dose of 50 milliroentgens per day is obtained with internal application of about 85 microcuries of $P^{32}$. The authors have used quantities of the order of 50 microcuries in their experiment and feel that for complete decay of the radioactive phosphorus this amount corresponds to a dose of 0.6 roentgen which they consider completely safe.—*Otto Glasser, Ph.D.*

WISHAM, L. H., YALOW, R. S., and FREUND, A. J. Consistency of clearance of radioactive sodium from human muscle. *Am. Heart J.*, June, 1951, *41*, 810–818.

A method for the measurement of effective blood flow using the clearance of radioactive sodium ($Na^{24}$) from tissue has been described (Kety, S. S. Measurement of regional circulation by the local clearance of radioactive sodium. *Am. Heart J.*, 1949, *38*, 321.). The value of this technique could be increased if it could be shown that the rate of clearance is reproducible within relatively narrow limits over an extended period of time.

The present study repeatedly determined clearance rate of radiosodium from gastrocnemius and biceps muscles of normal human subjects at rest, during moderate exercise, following fatiguing exercise, and during postural changes, over a period up to three months. Amounts of 0.05 to 0.1 cc. of isotonic sodium chloride solution containing between 1 and 4 microcuries of $Na^{24}$ were injected to a standard depth in the muscle belly (gastrocnemius or biceps). A Geiger-Müller counter was fixed in position over the injection site and counts made at intervals. The counting data were plotted on semilogarithmic paper as a function of time.

It is to be noted that the total counting rate over the injection site is made up of the following factors: (1) the natural background of the counter, (2) the counting rate resulting from the dispersal of $Na^{24}$ throughout the body via the blood stream, (3) the counting rate resulting from $Na^{24}$ spilled on the skin, (4) the counting rate resulting from $Na^{24}$ in the subcutaneous tissue deposited when the needle is withdrawn after injection is made, and (5) the counting rate of the $Na^{24}$ in the muscle.

The results of the normal subjects show that the rate of clearance remains constant within a relatively narrow range over long time periods. The clearance constant averages for the various individuals in the study were variable from individual to individual. Moderate exercise will significantly increase the rate of clearance of radiosodium from muscle within thirty minutes from the start of the excercise. Postural changes have no effect on the clearance rate.—*Harold Fulton, M.D.*

Semple, R., McDonald, L., and Ekins, R. P. Radioactive sodium ($Na^{24}$) in the measurement of local blood flow. *Am. Heart J.*, June, 1951, *41*, 803–809.

The authors use the method of Kety to determine whether the clearance rate of radioactive sodium ($Na^{24}$) from muscle after its intramuscular injection would measure muscle blood flow indirectly. An intramuscular injection of readily diffusible radioactive sodium is followed by serial counts (Geiger-Müller counter) which decrease along a single exponential curve which plotted semilogarithmically with respect to time should yield a straight line. The slope of this line is the quantitative measure of the total ability of the local circulation to remove and to supply freely diffusible substances.

Such serial counts on normal subjects and on subjects with peripheral vascular disease, all carrying out widely varying grades of exercise, all fell within the same range. In the light of these findings, the suggestion that this method might be used to assess the effect of therapy in peripheral vascular disease seems at present to be unjustified. It is thought that the relation between muscle blood flow and $Na^{24}$ clearance rate can only be established when the two have been correlated with simultaneous direct measurement of blood flow and estimation of $Na^{24}$ clearance. It appears from available evidence that there is no fixed relation between the two.—*Harold Fulton, M.D.*

## CHEMOTHERAPY

Esser, H., Ferenbach, H., and Schmengler, F. E. Zur Therapie der Boeckschen Erkrankung. (Treatment of Boeck's sarcoid.) *Deutsche med. Wchnschr.*, June 1, 1951, *76*, 740–742.

Experiences with 2 cases of Boeck's sarcoid of the lungs treated with pentamidine and stilbamidine are reported.

A favorable result was observed in a sixteen year old male, with the following clinical findings: A chest roentgenogram showed enlargement of the hilar shadows associated with small nodular densities in the lung fields. The right supraclavicular and axillary lymph nodes were enlarged. The Mantoux test was positive in 1:10. A biopsy showed Boeck's sarcoid. Pentamidine was given in daily doses of 50 to 100 mg. with a total dose of 1.5 gm. in $5\frac{1}{2}$ weeks. A marked roentgenological improvement was noted after seven doses (350 mg.) and four weeks later almost complete disappearance of the hilar and pulmonary lesions was found; the enlarged lymph nodes had also disappeared. Re-examination of the patient after two and eight months showed no recurrence.

A second case, a male thirty-six years old suffering from Boeck's sarcoid for three years, showed no response to 1.5 gm. of stilbamidine given in eighteen days. This is explained by the fact that the lesions were largely sclerosed, due in part to previous roentgen therapy.

The author concludes that young granulomatous forms of Boeck's sarcoid respond favorably to pentamidine, but sclerosed, fibrous forms show no change. He warns of a possible outbreak of tuberculous lesions under this treatment. This method of treatment seems to warrant further investigation.—*K. E. Matzinger, M.D.*

Haines, Richard D., Powell, W. N., and Bailey, Herbert A. Multiple myeloma: its treatment with urethane and ACTH. *South. M. J.*, June, 1951, *44*, 467–477.

Observations on the treatment of 5 cases of multiple myeloma and 1 case of solitary myeloma with urethane and ACTH are reported. The authors summarize their results as follows:

Two patients with multiple myeloma were treated with urethane alone. One patient showed subjective improvement with relief of bone pain and disappearance of daily fever, but died four months after treatment was begun. The other patient, who had a pathologic fracture of the third cervical vertebra when first seen, was relieved of bone pain and showed healing of his fracture. After seven months of urethane therapy he was able to return to a part-time position as a railroad employee.

Two patients with multiple myeloma were treated with ACTH alone. One showed considerable subjective improvement with relief of bone pain and roentgen evidence of callus formation about the site of a pathologic fracture of the right humerus. The other patient exhibited no subjective or objective evidence of benefit.

One patient was treated with both urethane and ACTH. She showed marked subjective improvement,

with relief of bone pain. There was alteration toward normal in her blood findings, both morphologic and chemical, and she was able to resume many of her former activities. The authors attribute most of her improvement to the use of urethane.

A patient with a solitary myeloma of the left ilium, treated with ACTH alone, revealed no definite evidence of improvement by control biopsy or roentgenographic study.

With both urethane and ACTH there was an inconstant change regarding the anemia, the hypercalcemia, and the hyperproteinemia.

At the present time, the authors believe that urethane is the drug of choice for the treatment of multiple myeloma. (Two grams of urethane daily, either tablet or liquid, has been the arbitrary dosage.) The production of gastrointestinal disturbance and leukopenia appear to be the chief untoward effects. Leukocyte counts should be done at weekly intervals until the patient's response to the drug is established. —*J. G. Snead, M.D.*

## MISCELLANEOUS

MARTIN, NOEL D., and SLATER, E. S. Direct tissue radioautography technique applied to teeth. *Science*, June 22, 1951, *113*, 721–722.

The authors investigated the permeability of dentine and enamel of the teeth to $P^{32}$ labeled $NaH_2PO_4$ following the treatment of the teeth by fluorides and other compounds.

They prepared two cavities in a tooth specimen. One was treated with 2 per cent NaF and 2 per cent $CaCl_2$ to form a precipitate of $CaF_2$ in the cavity. The other cavity was untreated and used as a control. In each cavity they placed 30 microcuries of $P^{32}$ and sealed the cavities.

After twenty-four hours a ground section of the tooth was prepared and film emulsion laid in contact with it. The resultant composite radioautograph and section showed a diffuse penetration of $P^{32}$ in the control cavity but the fluoride treated cavity had decreased the diffusion to a great extent.

The work seems to indicate the effect of a layer of calcium fluoride in decreasing the permeability of the dentine.—*R. A. Hays, M.D.*

MEEKER, IRVING A., JR., and GROSS, ROBERT E. Sterilization of frozen arterial grafts by high-voltage cathode-ray irradiation. *Surgery*, July, 1951, *30*, 19–28.

The authors realize a need for aseptic arterial grafts not as yet met by present day methods of sterilization. This procedure must insure the integrity of the donor segment. A more rapid and dependable method is their goal.

On the basis of the work done in conjunction with the food and drug industry and the results therein, they took their problem to Dr. John Trump who made possible research with high voltage cathode-ray beams.

The technical aspects of the cathode-ray generator are discussed.

A preliminary trial run and three experiments constituted the series of investigations.

The segments of 4 aortas were removed without regard to sepsis and without special preparation and irradiated at room temperature. The dose administered was 1.5 million roentgen equivalent physical (r.e.p.). There was immediate failure when these segments were transplanted due to intense radiation reaction and arterial thrombosis.

Then frozen aortic segments were used and the following experiments performed:

(1) *Irradiation of frozen, intentionally contaminated aortic segments which were subsequently cultured.* 125 aortic segments were placed in sealed polyethylene bags and contaminated with 8 different organisms. Prior to this, the bags containing the segments were frozen to −55°C. in a carbon dioxide refrigerator. These bags were irradiated within 3–4 hours with doses varying from 1.5–6.0 million r.e.p. Within two hours the specimens were thawed and cultured. There was growth from only three, at 2.0, 3.0 and 5.0 million r.e.p. respectively.

(2) *Irradiation of non-sterile frozen segments which were then transplanted.* 17 segments were exposed to 1.5 million r.e.p. and implanted one to five months later. 1.5 million r.e.p. was recommended as the minimum sterilizing dose for foodstuffs. There were no operative deaths. No antibiotics or anticoagulants were used. Except for two grafts with degenerative changes all were successful transplants.

(3) *Irradiation of frozen, intentionally contaminated segments with subsequent transplant.* Four dogs received segments irradiated with 1.5 million r.e.p. and 17 dogs received segments irradiated with 2.0 million r.e.p. One died because of dehiscence and hemorrhage; 7 were sacrificed and found to have intact grafts with small plaques in 2 cases; 13 are living and well. Eleven dogs received segments irradiated with 3.0 million r.e.p. and 11 with 4.0 million r.e.p. and are all well to date.

*The authors' conclusions.* Contaminated vascular segments can be sterilized with high voltage cathode rays, but in some instances damaged. There would seem to be a mean dosage somewhere between 1.5 and 3.0 million r.e.p.; 1.5 million r.e.p. at least is necessary. The grafts must be in a frozen state. The results compare favorably with their previous work in sterilization with a fluid medium technique. To date, two humans with coarctation of the aorta have received transplants and are well after two and six months respectively.—*F. W. O'Brien, Jr., M.D.*

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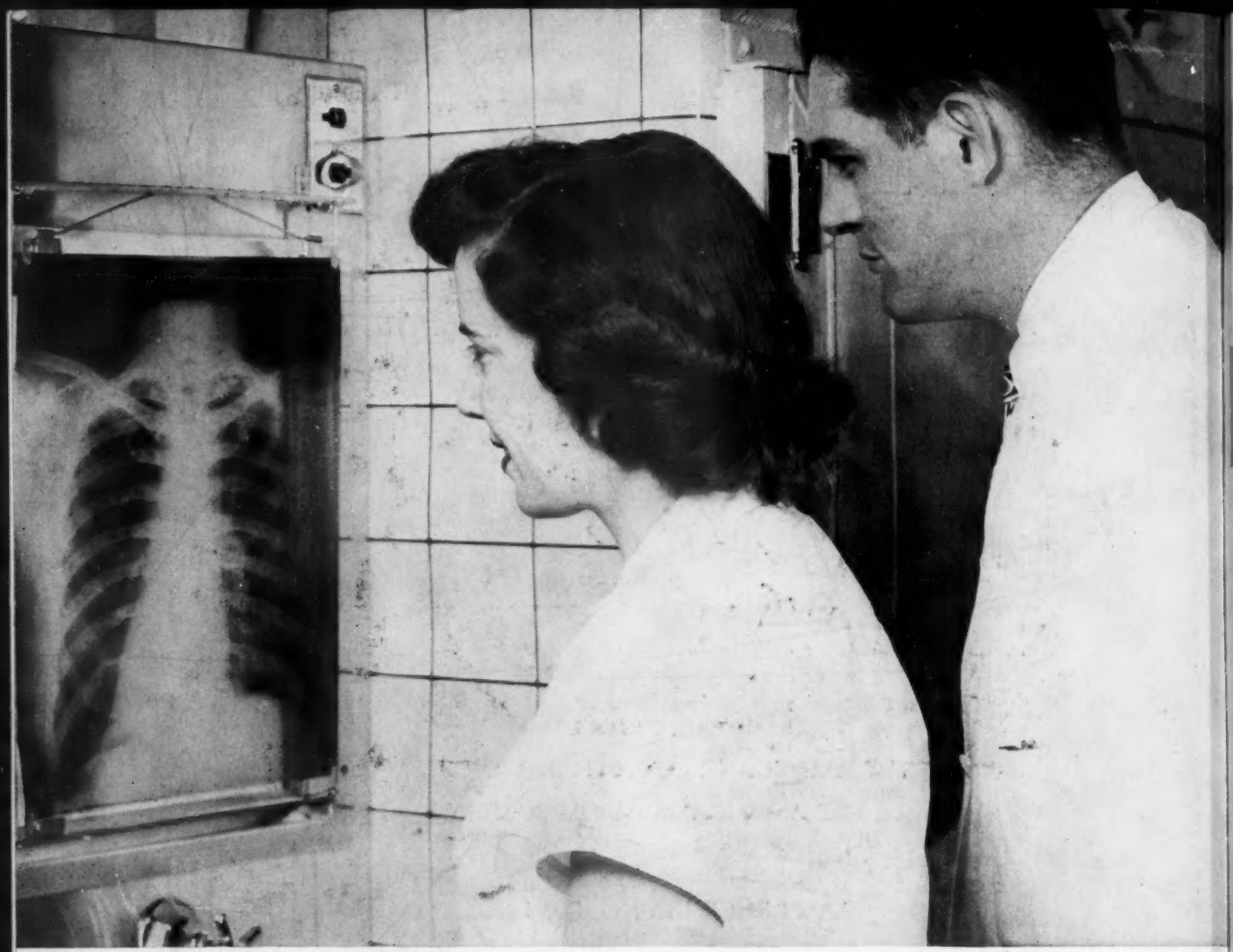

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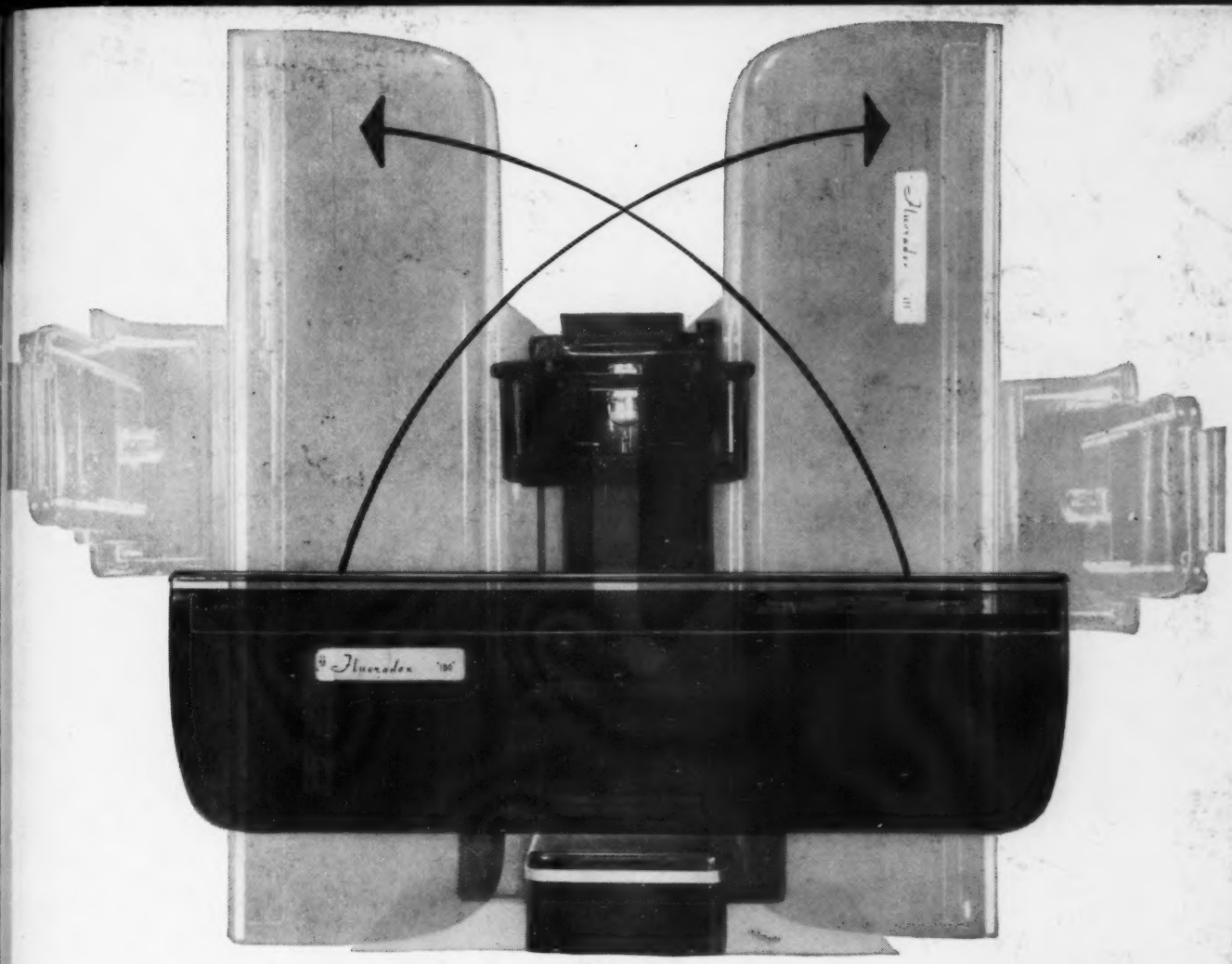


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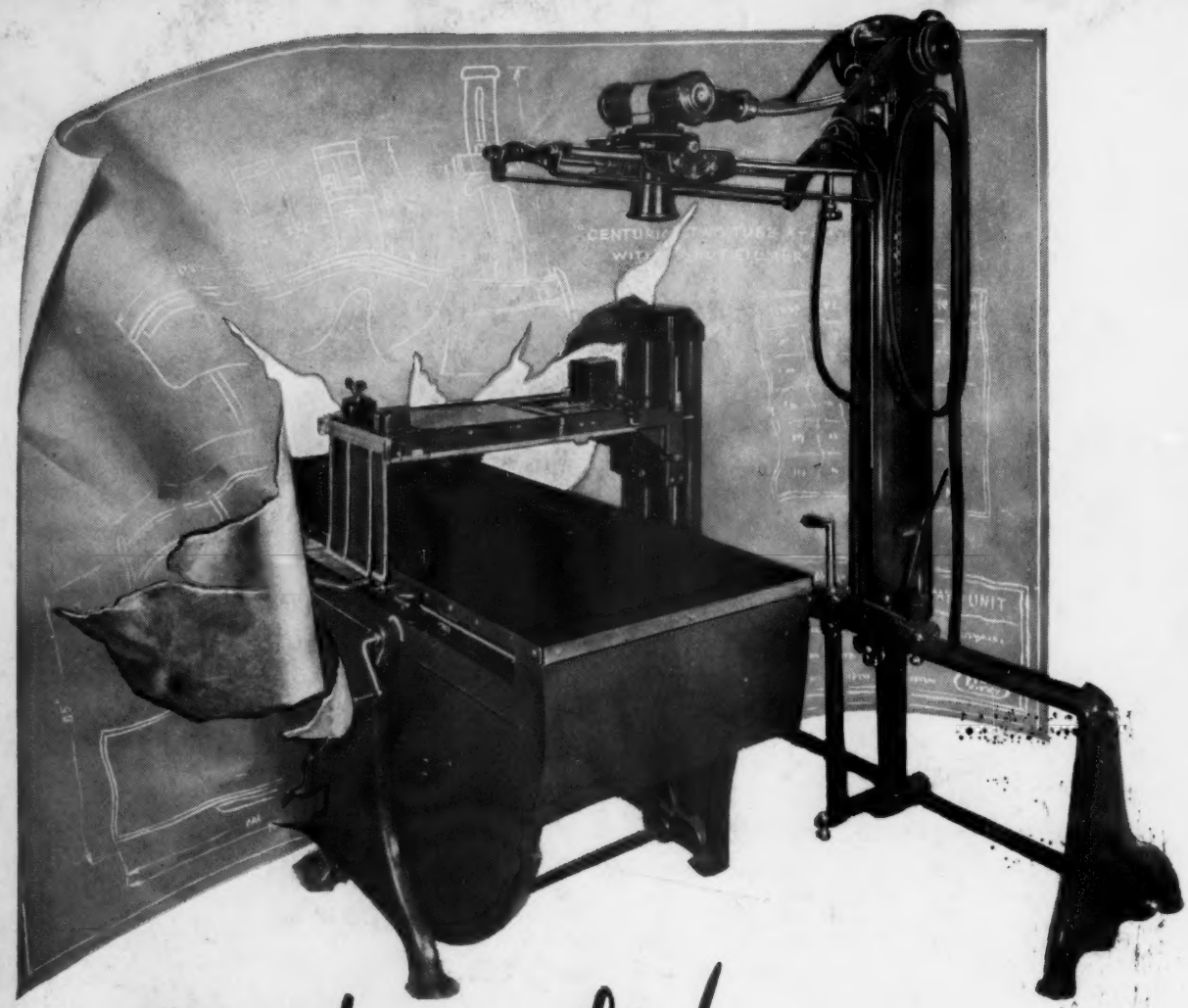

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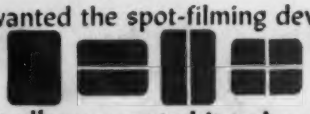
You wanted the spot-filming device to give you a selection of fields  (whole film, half film or four "spots").

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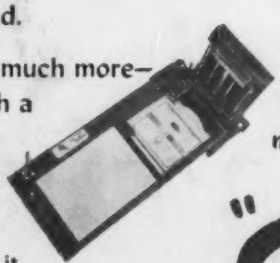

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